Table 13: **gp160**

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
gp160(32–44)	gp120(39–51)	EQLWVTVYYGVPV	Vaccine	murine(H-2^{bxk})	[Sastry1991]
Vaccine: *Vector/type:* peptide					
• Peptides induced T-cell proliferative response to immunizing peptide and to gp160					
gp160(38–48)	Env(45–55)	VYYGVPVWKEA	Vaccine	Rhesus macaque( )	[Nehete1993]
Vaccine: *Vector/type:* peptide					
• Synthetic peptide derived from conserved region of the HIV-1 envelope that stimulates a proliferative response in mice • Proliferative response to this peptide was observed in 3/3 immunized rhesus monkeys					
gp160(38–48)	Env(45–55)	VYYGVPVWKEA	HIV-1 infection	human, chimpanzee( )	[Nehete1998a]
• 7/9 HIV-infected chimpanzees and 8/17 HIV-positive humans exhibited positive proliferative responses to this conserved peptide (peptide 104) – no HIV negative individuals showed a response • This peptide, along with 4 other peptides from conserved regions of envelope, can induce proliferative responses to HIV and may be useful for vaccines • Peptide 104 elicited proliferative responses in inbred mouse strains and outbred rhesus monkeys in previous study by same group					
gp160(38–48)	gp120(45–55)	VYYGVPVWKEA	Vaccine	murine(H-$2^{bxk,sxd}$)	[Sastry1991]
Vaccine: *Vector/type:* peptide					
• Peptides induced T-cell proliferative response to immunizing peptide and to gp160					
gp160(41–54)	Env(48–60)	GVPVWKEATTLFC	Vaccine	Rhesus macaque( )	[Nehete1993]
Vaccine: *Vector/type:* peptide					
• Synthetic peptide derived from conserved region of the HIV-1 envelope that stimulates a proliferative response in mice • Despite the proliferative response to this peptide in mice, no response was observed in 3 rhesus monkeys					
gp160(41–54)	gp120(48–61)	GVPVWKEATTLFC	Vaccine	murine(H-2^{sxd})	[Sastry1991]
Vaccine: *Vector/type:* peptide					
• Peptides induced T-cell proliferative response to immunizing peptide and to gp160					
gp160(41–60)	gp120(40–59 89.6)	GVPVWREATTTLFCA-SDAKA	Vaccine	murine(H-2^{d})	[Dai2001]
Vaccine: *Vector/type:* recombinant protein *Strain:* 89.6 *HIV component:* gp120 *Stimulatory Agents:* mutant R192G heat-labile toxin from *E. coli* as adjuvant					

- Promiscuous immunodominant epitope in gp120 were mapped by overlapping peptides in CBA/J H-2^k and BALB/c H-2^d mice, and all were found to be in the outer domain, proximal to regions of structural disorder indicated by the crystal structure or by sequence divergence
- This peptide was recognized by 10/10 BALB/c with an average SI of 6.4, the strongest reaction among BALB/c mice, but not by CBA/J mice, but recognized well not by CBA/J mice, so is considered to be uniquely immunodominant for H-2^d
- Uniquely immunodominant sequences tended to be in the interior of the protein

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gp160(65–75) | gp120(72–82) | AHKVWATHACV | Vaccine | murine(H-2^{bxk,sxd}) | [Sastry1991]

Vaccine: *Vector/type:* peptide

- Peptides induced T-cell proliferative response to immunizing peptide and to gp160

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gp160(74–85) | gp120(74–85 LAI) | CVPTDPNPQEVV | HIV-1 infection | human( ) | [Schrier1989]

- Stimulates T-cell proliferation in HIV-infected donors

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gp160(74–85) | gp120(81–92) | CVPTNPVPQEVV | Vaccine | murine(H-2^{bxk,sxd}) | [Sastry1991]

Vaccine: *Vector/type:* peptide

- Peptides induced T-cell proliferative response to immunizing peptide and to gp160

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gp160(80–99) | gp120(51–70 HXB2) | NPQEVVLVNTENFNM-WKND | *in vitro* stimulation | human( ) | [LiPira1998]

- Clonal heterogeneity was broad for a recall response to tetanus toxoid or PPD, but oligoclonal to primary HIV antigens, dominated in this case by TCR Vβ 13 usage
- Donor of PBMC that recognized this epitope had HLA-DR2 and HLA-DR7

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gp160(81–100) | gp120(80–99 89.6) | PQEVVLGNVTENFNM-WKNNM | Vaccine | murine(H-2^k) | [Dai2001]

Vaccine: *Vector/type:* recombinant protein *Strain:* 89.6 *HIV component:* gp120 *Stimulatory Agents:* mutant R192G heat-labile toxin from *E. coli* as adjuvant

- Promiscuous immunodominant epitope in gp120 were mapped by overlapping peptides in CBA/J H-2^k and BALB/c H-2^d mice, and all were found to be in the outer domain, proximal to regions of structural disorder indicated by the crystal structure or by sequence divergence
- This peptide was recognized by 10/10 CBA/J mice with an average SI of 8.2, but not by BALB/c mice, so is considered to be uniquely immunodominant for H-2^k
- Uniquely immunodominant sequences tended to be in the interior of the protein

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gp160(92–101) | gp120(90–100 W6.ID) | YFNMWKNNMV | Vaccine | human( ) | [Jones1999]

Vaccine: *Vector/type:* recombinant protein *Strain:* W61D *HIV component:* gp120 *Stimulatory Agents:* QS21/MPL adjuvant

- An HIV seronegative volunteer was vaccinated with rgp120 and a QS21/MPL adjuvant and HIV-1 specific T-cell lines were isolated
- One T-cell clone reacts with two overlapping peptides, and the region of overlap is: YFNMWKNNMV
- The first 20-mer peptide that this clone reacts with is PQEVVLGNVTEYFNMWKNNMV, and the IIIB version of this peptide does not induce proliferation in the T-cell line that responds to the W61D version: IIIB: `------V----N-D----D--`

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gp160(92–111)	gp120(92–111 W6.ID)	YFNMWKNNMVDQMHE-Vaccine DIISL		human( )	[Jones1999]

Vaccine: *Vector/type:* recombinant protein *Strain:* W61D *HIV component:* gp120 *Stimulatory Agents:* QS21/MPL adjuvant

- An HIV seronegative volunteer was vaccinated with rgp120 and a QS21/MPL adjuvant and HIV-1 specific T-cell lines were isolated
- The IIIB version of this peptide does not induce proliferation in the T-cell line that responds to the W61D version of the peptide `N-D----D--E---------`
- Six T-cell lines react with this peptide, but some of these can also be stimulated by other gp120 peptides located in different regions of gp120

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gp160(101–126)	gp120(101–126)	VEQMHEDIISLWDQSL-KPCVKLTPLC	Vaccine	murine(H-2^k)	[Sjolander1996]

Vaccine: *Vector/type:* recombinant protein *HIV component:* gp160

- Study showing that T-cell determinants from glycoproteins can be dependent on the glycosylation of the protein

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gp160(102–114)	gp120(109–121)	EQMHEDIISLWDQ	Vaccine	murine(H-2^{bxk})	[Sastry1991]

Vaccine: *Vector/type:* peptide

- Peptides induced T-cell proliferative response to immunizing peptide and to gp160

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gp160(102–116)	gp160(109–123 IIIB)	EQMHEDIISLWDQSL	Vaccine	murine(H-2^d, H-2^b)	[Berzofsky1991, Berzofsky1991a]

Vaccine: *Vector/type:* recombinant protein *Strain:* IIIB *HIV component:* gp160 *Stimulatory Agents:* Freund's adjuvant

- B10.D2 (H-$2A^d$, E^d) and B10.A(R5) (H-$2A^b$, E^b) mice immunized with rec gp160 showed a proliferative response to EQMHEDIISLWDQSL
- EQMHEDIISLWDQSLKPCVK encompasses several murine Th epitopes including HEDIISLWDQSLK and is referred to as a "multideterminant region" or cluster peptide

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gp160(102–116)	gp120(109–123 IIIB)	EQMHEDIISLWDQSL	Vaccine	murine(H-$2^{d,i5}$)	[Hale1989]

Vaccine: *Vector/type:* recombinant protein *Strain:* IIIB *HIV component:* gp160

- Six multideterminant helper T-cell regions are recognized by mice of three or four MHC types

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gp160(102–121)	gp160(109–128 IIIB)	EQMHEDIISLWDQSLK-PCVK	HIV-1 infection, Vaccine	human, murine(H-2^k, H-2^s)	[Berzofsky1991, Berzofsky1991a]

Vaccine: *Vector/type:* recombinant protein *Strain:* IIIB *HIV component:* gp160 *Stimulatory Agents:* Freund's adjuvant

- EQMHEDIISLWDQSLKPCVK encompasses several murine Th epitopes and is referred to as a "multideterminant region" or cluster peptide
- Six multideterminant region cluster peptides were evaluated Th responses in different MHC/HLA backgrounds after vaccination of mice with gp160, or in infected people
- This cluster peptide elicited proliferative responses in cells from vaccinated B10.BR mice (H-2A^k, E^k) and B10.S(9R) mice (H-2A^s, E^s), while shorter peptides from within this region stimulated H-2^k, H-2^d and H-2^b responses, but not H-2^s
- IL-2 production was observed in response to this peptide in 64% (23/36) of asymptomatic HIV-infected individuals

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gp160(105–117)	gp120(112–124 IIIB)	HEDIISLWDQSLK	HIV-1 infection	human( )	[Clerici1997]

- Epitope name: T2. Used in a study of pentoxifylline's influence on HIV specific T-cells

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gp160(105–117)	gp120(112–124 BH10)	HEDIISLWDQSLK	Vaccine	human( )	[Berzofsky1988]

Vaccine: *Vector/type:* vaccinia *Strain:* IIIB *HIV component:* gp160

- Epitope name: T2. Proliferative response to T1 and T2 peptides in 14 immunized, uninfected humans

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gp160(105–117)	gp120(112–124 IIIB)	HEDIISLWDQSLK	HIV-1 infection	human( )	[Clerici1989]

- Epitope name: T2. IL-2 production detection of Th lymphocytes from asymptomatic HIV-positive individuals

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gp160(105–117)	gp120(112–124 IIIB)	HEDIISLWDQSLK	HIV-1 infection	human( )	[Clerici1991a]

- Epitope name: T2. Peptides stimulate Th cell function and CTL activity in similar patient populations

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gp160(105–117)	gp120(112–124)	HEDIISLWDQSLK	Vaccine	human( )	[Clerici1991b]

Vaccine: *Vector/type:* recombinant protein *Strain:* IIIB *HIV component:* gp160

- Epitope name: T2. Immunizing uninfected individuals with rgp160 results in stronger Th response than does natural infection

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gp160(105–117)	gp120(112–124 IIIB)	HEDIISLWDQSLK	HIV-1 exposed seronegative	human( )	[Clerici1992]

- Epitope name: T2. Cell-mediated immune response to HIV-1 peptides in HIV-1 exposed seronegative men

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gp160(105–117)	gp120(112–124 IIIB)	HEDIISLWDQSLK	Vaccine	Rhesus macaque( )	[Hosmalin1991]

Vaccine: *Vector/type:* peptide prime with protein boost *Strain:* IIIB *HIV component:* gp160

- Epitope name: T2. Peptide priming to induce T-cell help enhances antibody response to gp160 immunization

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gp160(105–117)	gp120(112–124 IIIB)	HEDIISLWDQSLK	HIV-1 exposed seronegative	human( )	[Pinto1995a]

- Epitope name: T2. CTL activity analyzed in parallel with Th reactivity in exposed but uninfected health care workers

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gp160(105–117)	gp120(112–124 IIIB)	HEDIISLWDQSLK	HIV-1 exposed seronegative	human( )	[Kaul1999a]

- Epitope name: T2. Kenyan sex workers that remained seronegative were found to frequently have HIV-env peptide specific Th responses detected by an IL-2 assay (11/20 cases) and mucosal genital tract anti-HIV IgA (16/21 cases)
- The helper epitopes used in this study were noted to be previously described [Clerici1989], and were not explicitly described in [Kaul1999a]

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gp160(105–117)	gp120( )	HEDIISLWDQSLK	HIV-1 exposed seronegative, HIV-1 infection	human( )	[Kuhn2001]

- Epitope name: T2. In a S. African perinatal transmission study, 33% (33/86) of cord blood samples from infants with seropositive mothers produced T-helper responses (measured by a bioassay measuring IL-2 production in a murine cell line and confirmed with a proliferation assay) against a peptide cocktail containing Th epitopes P18 MN, P18 IIIB, T1, T2, and TH4
- The mothers were predominantly infected subtype C but the T-helper response was detectable in a number of cord blood samples despite using peptides based on B subtype reagents
- 3/33 infants with cord blood T-helper responses to Env were infected *in utero*, 2/33 were lost to follow up, and 28/33 were not infected – 6/53 of the infants with cord blood that was unresponsive to Env peptide stimulation were infected before delivery, and 8/47 contracted HIV intrapartum or via breast-feeding
- Measurable HIV specific T-helper responses elicited in the immunologically immature newborn, possibly in response to *in utero* exposure, are associated with a protective natural immunity that helps block mother-infant transmission of HIV-1

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gp160(105–117)	gp120(112–124 IIIB)	HEDIISLWDQSLK	Vaccine	murine(H-2^k)	[Hale1989]

Vaccine: *Strain:* IIIB *HIV component:* gp160

- Epitope name: T2. Six multideterminant helper T-cell regions are recognized by mice of three or four MHC types

---

gp160(105–117)	gp160(112–124 IIIB)	HEDIISLWDQSLK	Vaccine	murine(H-2^k)	[Berzofsky1991, Berzofsky1991a]

Vaccine: *Vector/type:* recombinant protein *Strain:* IIIB *HIV component:* gp160 *Stimulatory Agents:* Freund's adjuvant

- B10.BR (H-2A^k, E^k) mice immunized with rec gp160 showed a strong proliferative response to three overlapping peptides, QMHEDIISLWDQSL, HEDIISLWDQSLK, and DIISLWDQSLKPCVK, and HEDIISLWDQSLK is common to between them
- EQMHEDIISLWDQSLKPCVK encompasses several murine Th epitopes including HEDIISLWDQSLK and is referred to as a "multideterminant region" or cluster peptide

---

gp160(105–117)	gp120(112–124 BH10)	HEDIISLWDQSLK	computer prediction	murine(H-$2^{k,s}$)	[Cease1987a]

- Epitope name: T2. 1 of 2 functional epitopes identified using an amphipathic helix epitope prediction algorithm

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gp160(105–123)	gp120(112–130 IIIB)	HEDIISLWDQSLKPCV-KLT		human( )	[Furci1997]

- 9/11 exposed-uninfected individuals in this study had a proliferative response to a C5 peptide, but none reacted with this previously defined epitope

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gp160(108–119) gp120(108–119 LAI) IISLWDQSLKPC HIV-1 infection human( ) [Schrier1989]

- Stimulates T-cell proliferation in HIV-infected donors

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gp160(110–125) gp120(110–125) SLWDQSLKPCVKLTPL HIV-1 infection human( ) [Caruso1997]

- As HIV-1-infected individuals progress to disease, T-cells show reduced ability to proliferate in response to HIV antigen, but retain the ability to express the activation antigens CD25 and CD71
- The ability to express activation markers in response to HIV is retained, but the response to tetanus toxoid recall antigen is lost
- This study investigated CD25 and CD71 expression in PBMC from patients at various stages of progression, measuring the response to *in vitro* stimulation by peptide cocktail containing four antigenic Env peptides, or p17 and p24

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gp160(111–123) gp120(118–130) LWDQSLKPCVKLT Vaccine Rhesus macaque( ) [Nehete1993]

Vaccine: *Vector/type:* peptide

- Synthetic peptide derived from conserved region of the HIV-1 envelope that stimulates a proliferative response in mice
- Proliferative response to this peptide was observed in 3/3 immunized rhesus monkeys

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gp160(112–141) gp120(112–141 NL43) WDQSLKPCVKLTPLC-VSLKCTDLGNATNTN Vaccine human( ) [Sitz1999]

Vaccine: *Vector/type:* recombinant protein *Strain:* NL43 *HIV component:* gp120, gp160

- There was a great breadth of proliferative response to Env peptides in 19 HIV-1 infected rgp160 and 17 HIV-1 infected rgp120 vaccine recipients
- Over 35% of vaccinees had a stimulation index of greater than 5 to this peptide

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gp160(115–126) gp120(115–126 LAI) SLKPCVKLTPLC HIV-1 infection human( ) [Schrier1989]

- Stimulates T-cell proliferation in HIV-infected donors

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gp160(115–129) gp120(115–129 LAI) SLKPCVKLTPLCVSL Peptide-HLA interaction human(HLA-DR) [Gaudebout1997]

- Peptide bound to both HLA-DR*1101 and HLA-DR*0401 with high affinity
- Because of the distinctive binding pockets of HLA-DR*1101 and HLA-DR*0401, peptides that bound both were considered candidates for promiscuous HLA-DR binding

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gp160(138–159) gp120(141–160 W6.ID) TTSNGWTGEIRKGEIK-NCSF Vaccine human( ) [Jones1999]

Vaccine: *Vector/type:* recombinant protein *Strain:* W61D *HIV component:* gp120 *Stimulatory Agents:* QS21/MPL adjuvant

- An HIV seronegative volunteer was vaccinated with rgp120 and a QS21/MPL adjuvant and HIV-1 specific T-cell lines were isolated
- The IIIB version of this peptide does not induce proliferation in the T-cell line that responds to the W61D version of the peptide: IIIB: `---SSGRMIME---------`

gp160(147–168)	gp120(152–173 NL43)	MMMEKGEIKNCSFNI-STSIRGK	Vaccine	human( )	[Sitz1999]

Vaccine: *Vector/type:* recombinant protein *Strain:* NL43 *HIV component:* gp120, gp160

- There was a great breadth of proliferative response to Env peptides in 19 HIV-1 infected rgp160 and 17 HIV-1 infected rgp120 vaccine recipients
- Over 50% of vaccinees had a stimulation index of greater than 5 to this peptide

gp160(155–169)	Env( )	KNCSFNITTELIDKK	Vaccine	murine(H-2 IA^b)	[Surman2001]

Vaccine: *Vector/type:* DNA, vaccinia, recombinant protein *Strain:* 1007 (clade B), UG92005 (clade D) *HIV component:* gp140 *Stimulatory Agents:* Freund's adjuvant

- This epitope is located in the V2 region of UG92005 (UG, clade D) and the hybridoma that recognized it used Vβ5
- C57BL/6 mice were immunized with a prime-boost strategy involving three HIV-1 Env antigens: Mice were primed with DNA given i.m., 3-4 weeks later boosted with VV, and 3-4 weeks later boosted again with purified protein in Freund's adjuvant
- The vaccinia construct is a pSC11-based VV vector with the first 38 amino acids contributed by BH10 and the rest of gp120 and gp41 by the vaccine strain, the DNA construct is in the pJW4303 vector with a CMV promotor, and the purified protein is expressed from the pJW4303 vector transfected into CHO-K1 cells
- Ten days after the final boost, hybridomas were made and tested for IL-2 production using either B6 spleen cells or H-2 IA^b transfected L cells as targets and Vβ usage was determined
- Mice were immunized with an Env from either one of two clades: HIV-1 1007, a clade B strain isolated from an individual from Memphis Tennesee, and HIV-1 92UG005, a clade D strain isolated from Uganda in 1992 through the WHO
- 80 unique clonotypes were characterized from six mice
- H-2 IA^b restricted T-helper epitopes were concentrated in 5 distinct regions within the Env sequence (2 clonotype responses in V2, 26 in C2, 22 in V3, 23 in V4C4, and 7 in gp41
- Epitopes hotspots tended to be proximal to heavily glycosylated regions of the Env sequence, in exposed, non-helical strands of the protein – the non-uniform localization may be influenced by differential antigen processing and the glycosylation site proximity may allow binding to lectins and promote trafficking through processing pathways

gp160(155–169)	gp120(160–174 LAI)	KNCSFNISTSIRGKV		human(HLA-DR)	[Gaudebout1997]

- Peptide binds to both HLA-DR*1101 and HLA-DR*0401 with high affinity
- Because of the distinctive binding pockets of HLA-DR*1101 and HLA-DR*0401, peptides that bound both were considered candidates for promiscuous HLA-DR binding

gp160(162–181)	gp120(162–181 IIIB)	STSIRGKVQKEYAFFY-KLDI	Vaccine	Rhesus macaque( )	[Lekutis1997a]

Vaccine: *Vector/type:* DNA *Strain:* IIIB *HIV component:* Env

- HIV-1 env DNA vaccine induced Th cell response to this epitope in a rhesus monkeys

gp160(169–189)	gp120(141–160 W6.ID)	VQKEYALFYNLDVVPI-DDDNA	Vaccine	human( )	[Jones1999]

Vaccine: *Vector/type:* recombinant protein *Strain:* W61D *HIV component:* gp120 *Stimulatory Agents:* QS21/MPL adjuvant

- An HIV seronegative volunteer was vaccinated with rgp120 and a QS21/MPL adjuvant and HIV-1 specific T-cell lines were isolated
- The IIIB version of this peptide does not induce proliferation in the T-cell line that responds to the W61D version of the peptide `------F--K--II---N-TT`
- Two T-cell lines react specifically with this peptide

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gp160(172–191)	gp120(172–191 IIIB)	EYAFFYKLDIIPIDNDT-TSY	Vaccine	Rhesus macaque( )	[Lekutis1997a]

Vaccine: *Vector/type:* DNA *Strain:* IIIB *HIV component:* Env

- HIV-1 env DNA vaccine induced Th cell response to this epitope in a rhesus monkey

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gp160(175–189)	Env( )	LFYKLDVVQIDNSTN	Vaccine	murine(H-2 IA^b)	[Surman2001]

Vaccine: *Vector/type:* DNA, vaccinia, recombinant protein *Strain:* 1007 (clade B), UG92005 (clade D) *HIV component:* gp140 *Stimulatory Agents:* Freund's adjuvant

- This epitope is located in the V2 region of UG92005 (UG, clade D) and the Vβ usage of the TCR was not determined
- C57BL/6 mice were immunized with a prime-boost strategy involving three HIV-1 Env antigens: Mice were primed with DNA given i.m., 3-4 weeks later boosted with VV, and 3-4 weeks later boosted again with purified protein in Freund's adjuvant
- The vaccinia construct is a pSC11-based VV vector with the first 38 amino acids contributed by BH10 and the rest of gp120 and gp41 by the vaccine strain, the DNA construct is in the pJW4303 vector with a CMV promotor, and the purified protein is expressed from the pJW4303 vector transfected into CHO-K1 cells
- Ten days after the final boost, hybridomas were made and tested for IL-2 production using either B6 spleen cells or H-2 IA^b transfected L cells as targets and Vβ usage was determined
- Mice were immunized with an Env from either one of two clades: HIV-1 1007, a clade B strain isolated from an individual from Memphis Tennesee, and HIV-1 92UG005, a clade D strain isolated from Uganda in 1992 through the WHO
- 80 unique clonotypes were characterized from six mice
- H-2 IA^b restricted T-helper epitopes were concentrated in 5 distinct regions within the Env sequence (2 clonotype responses in V2, 26 in C2, 22 in V3, 23 in V4C4, and 7 in gp41
- Epitopes hotspots tended to be proximal to heavily glycosylated regions of the Env sequence, in exposed, non-helical strands of the protein – the non-uniform localization may be influenced by differential antigen processing and the glycosylation site proximity may allow binding to lectins and promote trafficking through processing pathways

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gp160(185–215)	gp120(191–220 NL43)	NDTTSYTLTSCNTSVIT-QACPKVSFEPIPI	Vaccine	human( )	[Sitz1999]

Vaccine: *Vector/type:* recombinant protein *Strain:* NL43 *HIV component:* gp120, gp160

- There was a great breadth of proliferative response to Env peptides in 19 HIV-1 infected rgp160 and 17 HIV-1 infected rgp120 vaccine recipients

- Over 30% of vaccinees had a stimulation index of greater than 5 to this peptide

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gp160(188–207) | gp120(190–209 89.6) | NTKYRLISCNTSVITQ-ACPK | Vaccine | murine(H-2^k) | [Dai2001]

Vaccine: *Vector/type:* recombinant protein *Strain:* 89.6 *HIV component:* gp120 *Stimulatory Agents:* mutant R192G heat-labile toxin from *E. coli* as adjuvant

- Promiscuous immunodominant epitope in gp120 were mapped by overlapping peptides in CBA/J H-2^k and BALB/c H-2^d mice, and all were found to be in the outer domain, proximal to regions of structural disorder indicated by the crystal structure or by sequence divergence
- This peptide was recognized by 9/10 CBA/J mice with an average SI of 9.8, one of the two immunodominant peptides in CBA/J mice, and not by BALB/c mice, so is considered to be uniquely immunodominant for H-2^k
- Uniquely immunodominant sequences tended to be in the interior of the protein

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gp160(193–218) | gp120(193–218) | LTSCNSVITQACPKVS-FEPIPIHYC | Vaccine | murine(H-2^{d,b}) | [Sjolander1996]

Vaccine: *Vector/type:* recombinant protein *HIV component:* gp160

- Study showing that T-cell determinants from glycoproteins can be dependent on the glycosylation of the protein

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gp160(198–212) | Env( ) | TSVITQACPKVSFEP | Vaccine | murine(H-2 IA^b) | [Surman2001]

Vaccine: *Vector/type:* DNA, vaccinia, recombinant protein *Strain:* 1007 (clade B), UG92005 (clade D) *HIV component:* gp140 *Stimulatory Agents:* Freund's adjuvant

- This epitope is located in the C2 region of 1007 (US, clade B) and the Vβ usage of the TCRs for two clonotypes was Vβ3 and Vβ8.1-2
- C57BL/6 mice were immunized with a prime-boost strategy involving three HIV-1 Env antigens: Mice were primed with DNA given i.m., 3-4 weeks later boosted with VV, and 3-4 weeks later boosted again with purified protein in Freund's adjuvant
- The vaccinia construct is a pSC11-based VV vector with the first 38 amino acids contributed by BH10 and the rest of gp120 and gp41 by the vaccine strain, the DNA construct is in the pJW4303 vector with a CMV promotor, and the purified protein is expressed from the pJW4303 vector transfected into CHO-K1 cells
- Ten days after the final boost, hybridomas were made and tested for IL-2 production using either B6 spleen cells or H-2 IA^b transfected L cells as targets and Vβ usage was determined
- Mice were immunized with an Env from either one of two clades: HIV-1 1007, a clade B strain isolated from an individual from Memphis Tennesee, and HIV-1 92UG005, a clade D strain isolated from Uganda in 1992 through the WHO
- 80 unique clonotypes were characterized from six mice
- H-2 IA^b restricted T-helper epitopes were concentrated in 5 distinct regions within the Env sequence (2 clonotype responses in V2, 26 in C2, 22 in V3, 23 in V4C4, and 7 in gp41
- Epitopes hotspots tended to be proximal to heavily glycosylated regions of the Env sequence, in exposed, non-helical strands of the protein – the non-uniform localization may be influenced by differential antigen processing and the glycosylation site proximity may allow binding to lectins and promote trafficking through processing pathways

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gp160(199–211)	Env(204–216)	SVITQACSKVSFE	Vaccine	Rhesus macaque( )	[Nehete1993]

Vaccine: *Vector/type:* peptide

- Synthetic peptide derived from conserved region of the HIV-1 envelope that stimulates a proliferative response in mice
- A weak or transient proliferative response to this peptide was observed in 3/3 immunized rhesus monkeys

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gp160(199–211)	Env(204–216)	SVITQACSKVSFE	HIV-1 infection	human, chimpanzee( )	[Nehete1998a]

- HIV-infected chimpanzees and HIV-positive patients show positive proliferative responses to multiple peptides from five conserved regions of the HIV-1 Env

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gp160(199–211)	gp120(204–216)	SVITQACSKVSFE	Vaccine	murine(H-2^{bxk,sxd})	[Sastry1991]

Vaccine: *Vector/type:* peptide

- Peptides induced T-cell proliferative response in mice representing four haplotypes

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gp160(200–214)	gp120(205–219 LAI)	VITQACPKVSFEPIP	Peptide-HLA interaction	human(HLA-DR)	[Gaudebout1997]

- Peptide binds to both HLA-DR*1101 and HLA-DR*0401 with high affinity
- Because of the distinctive binding pockets of HLA-DR*1101 and HLA-DR*0401, peptides that bound both were considered candidates for promiscuous HLA-DR binding

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gp160(201–212)	Env( )	ITQACPKVSFEP	Vaccine	murine(H-2 IA^b)	[Surman2001]

Vaccine: *Vector/type:* DNA, vaccinia, recombinant protein *Strain:* 1007 (clade B), UG92005 (clade D) *HIV component:* gp140 *Stimulatory Agents:* Freund's adjuvant

- This epitope is located in the C2 region of 1007 (US, clade B) and the Vβ usage of the TCR was Vβ3
- The epitope described here is the region of overlap of two 15 mers that were both able to stimulate IL-2 production from the hybridoma (TSVITQACPKVSFEP and ITQACPKVSFEPIPI)
- C57BL/6 mice were immunized with a prime-boost strategy involving three HIV-1 Env antigens: Mice were primed with DNA given i.m., 3-4 weeks later boosted with VV, and 3-4 weeks later boosted again with purified protein in Freund's adjuvant
- The vaccinia construct is a pSC11-based VV vector with the first 38 amino acids contributed by BH10 and the rest of gp120 and gp41 by the vaccine strain, the DNA construct is in the pJW4303 vector with a CMV promotor, and the purified protein is expressed from the pJW4303 vector transfected into CHO-K1 cells
- Ten days after the final boost, hybridomas were made and tested for IL-2 production using either B6 spleen cells or H-2 IA^b transfected L cells as targets and Vβ usage was determined
- Mice were immunized with an Env from either one of two clades: HIV-1 1007, a clade B strain isolated from an individual from Memphis Tennesee, and HIV-1 92UG005, a clade D strain isolated from Uganda in 1992 through the WHO
- 80 unique clonotypes were characterized from six mice
- H-2 IA^b restricted T-helper epitopes were concentrated in 5 distinct regions within the Env sequence (2 clonotype responses in V2, 26 in C2, 22 in V3, 23 in V4C4, and 7 in gp41
- Epitopes hotspots tended to be proximal to heavily glycosylated regions of the Env sequence, in exposed, non-helical strands of the protein – the non-uniform localization may be influenced by differential antigen processing and the glycosylation site proximity may allow binding to lectins and promote trafficking through processing pathways

gp160(201–215) Env( ) TSVITQACPKVSFEPIPI Vaccine murine(H-2 IA^b) [Surman2001]

Vaccine: *Vector/type:* DNA, vaccinia, recombinant protein *Strain:* 1007 (clade B), UG92005 (clade D) *HIV component:* gp140 *Stimulatory Agents:* Freund's adjuvant

- This epitope is located in the C2 region of 1007 (US, clade B) and the Vβ usage of the TCR was Vβ6
- C57BL/6 mice were immunized with a prime-boost strategy involving three HIV-1 Env antigens: Mice were primed with DNA given i.m., 3-4 weeks later boosted with VV, and 3-4 weeks later boosted again with purified protein in Freund's adjuvant
- The vaccinia construct is a pSC11-based VV vector with the first 38 amino acids contributed by BH10 and the rest of gp120 and gp41 by the vaccine strain, the DNA construct is in the pJW4303 vector with a CMV promotor, and the purified protein is expressed from the pJW4303 vector transfected into CHO-K1 cells
- Ten days after the final boost, hybridomas were made and tested for IL-2 production using either B6 spleen cells or H-2 IA^b transfected L cells as targets and Vβ usage was determined
- Mice were immunized with an Env from either one of two clades: HIV-1 1007, a clade B strain isolated from an individual from Memphis Tennesee, and HIV-1 92UG005, a clade D strain isolated from Uganda in 1992 through the WHO
- 80 unique clonotypes were characterized from six mice
- H-2 IA^b restricted T-helper epitopes were concentrated in 5 distinct regions within the Env sequence (2 clonotype responses in V2, 26 in C2, 22 in V3, 23 in V4C4, and 7 in gp41
- Epitopes hotspots tended to be proximal to heavily glycosylated regions of the Env sequence, in exposed, non-helical strands of the protein – the non-uniform localization may be influenced by differential antigen processing and the glycosylation site proximity may allow binding to lectins and promote trafficking through processing pathways

gp160(206–220) Env( ) PKVSFEPIPIHYCAP Vaccine murine(H-2 IA^b) [Surman2001]

Vaccine: *Vector/type:* DNA, vaccinia, recombinant protein *Strain:* 1007 (clade B), UG92005 (clade D) *HIV component:* gp140 *Stimulatory Agents:* Freund's adjuvant

- This epitope is located in the C2 region of 1007 (US, clade B) and 12 hybridomas recognized the peptide with Vβ usage of Vβ4, 6, 7, 8.1-2, 8.3, 11, 12 and others not determined
- C57BL/6 mice were immunized with a prime-boost strategy involving three HIV-1 Env antigens: Mice were primed with DNA given i.m., 3-4 weeks later boosted with VV, and 3-4 weeks later boosted again with purified protein in Freund's adjuvant
- The vaccinia construct is a pSC11-based VV vector with the first 38 amino acids contributed by BH10 and the rest of gp120 and gp41 by the vaccine strain, the DNA construct is in the pJW4303 vector with a CMV promotor, and the purified protein is expressed from the pJW4303 vector transfected into CHO-K1 cells
- Ten days after the final boost, hybridomas were made and tested for IL-2 production using either B6 spleen cells or H-2 IA^b transfected L cells as targets and Vβ usage was determined
- Mice were immunized with an Env from either one of two clades: HIV-1 1007, a clade B strain isolated from an individual from Memphis Tennesee, and HIV-1 92UG005, a clade D strain isolated from Uganda in 1992 through the WHO
- 80 unique clonotypes were characterized from six mice
- H-2 IA^b restricted T-helper epitopes were concentrated in 5 distinct regions within the Env sequence (2 clonotype responses in V2, 26 in C2, 22 in V3, 23 in V4C4, and 7 in gp41

- Epitopes hotspots tended to be proximal to heavily glycosylated regions of the Env sequence, in exposed, non-helical strands of the protein – the non-uniform localization may be influenced by differential antigen processing and the glycosylation site proximity may allow binding to lectins and promote trafficking through processing pathways

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gp160(206–230) gp120(206–230) PKVSFEPIPIHYCAPAG-FAILKCNN Vaccine murine(H-$2^{d,b}$) [Sjolander1996]

Vaccine: *Vector/type:* recombinant protein *HIV component:* gp160

- Study showing that T-cell determinants from glycoproteins can be dependent on the glycosylation of the protein

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gp160(208–220) Env( ) ITFEPIPIHYC Vaccine murine(H-2 IA^b) [Surman2001]

Vaccine: *Vector/type:* DNA, vaccinia, recombinant protein *Strain:* 1007 (clade B), UG92005 (clade D) *HIV component:* gp140 *Stimulatory Agents:* Freund's adjuvant

- This epitope is located in the C2 region of UG92005 (UG, clade D) and its was recognized by two hybridomas with Vβ usage Vβ12 and not determined
- The epitope described here is the region of overlap of two 15 mers that were both able to stimulate IL-2 production from the hybridoma (PKITFEPIPIHYCAP and ITFEPIPIHYCAPAG)
- C57BL/6 mice were immunized with a prime-boost strategy involving three HIV-1 Env antigens: Mice were primed with DNA given i.m., 3-4 weeks later boosted with VV, and 3-4 weeks later boosted again with purified protein in Freund's adjuvant
- The vaccinia construct is a pSC11-based VV vector with the first 38 amino acids contributed by BH10 and the rest of gp120 and gp41 by the vaccine strain, the DNA construct is in the pJW4303 vector with a CMV promotor, and the purified protein is expressed from the pJW4303 vector transfected into CHO-K1 cells
- Ten days after the final boost, hybridomas were made and tested for IL-2 production using either B6 spleen cells or H-2 IA^b transfected L cells as targets and Vβ usage was determined
- Mice were immunized with an Env from either one of two clades: HIV-1 1007, a clade B strain isolated from an individual from Memphis Tennesee, and HIV-1 92UG005, a clade D strain isolated from Uganda in 1992 through the WHO
- 80 unique clonotypes were characterized from six mice
- H-2 IA^b restricted T-helper epitopes were concentrated in 5 distinct regions within the Env sequence (2 clonotype responses in V2, 26 in C2, 22 in V3, 23 in V4C4, and 7 in gp41
- Epitopes hotspots tended to be proximal to heavily glycosylated regions of the Env sequence, in exposed, non-helical strands of the protein – the non-uniform localization may be influenced by differential antigen processing and the glycosylation site proximity may allow binding to lectins and promote trafficking through processing pathways

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gp160(208–222) Env( ) ITFEPIPIHYCAPAG Vaccine murine(H-2 IA^b) [Surman2001]

Vaccine: *Vector/type:* DNA, vaccinia, recombinant protein *Strain:* 1007 (clade B), UG92005 (clade D) *HIV component:* gp140 *Stimulatory Agents:* Freund's adjuvant

- This epitope is located in the C2 region of UG92005 (UG, clade D) and it was recognized by five hybridomas with Vβ usage Vβ5, 8.2, 12 and not determined
- C57BL/6 mice were immunized with a prime-boost strategy involving three HIV-1 Env antigens: Mice were primed with DNA given i.m., 3-4 weeks later boosted with VV, and 3-4 weeks later boosted again with purified protein in Freund's adjuvant

- The vaccinia construct is a pSC11-based VV vector with the first 38 amino acids contributed by BH10 and the rest of gp120 and gp41 by the vaccine strain, the DNA construct is in the pJW4303 vector with a CMV promotor, and the purified protein is expressed from the pJW4303 vector transfected into CHO-K1 cells
- Ten days after the final boost, hybridomas were made and tested for IL-2 production using either B6 spleen cells or H-2 IA^b transfected L cells as targets and Vβ usage was determined
- Mice were immunized with an Env from either one of two clades: HIV-1 1007, a clade B strain isolated from an individual from Memphis Tennesee, and HIV-1 92UG005, a clade D strain isolated from Uganda in 1992 through the WHO
- 80 unique clonotypes were characterized from six mice
- H-2 IA^b restricted T-helper epitopes were concentrated in 5 distinct regions within the Env sequence (2 clonotype responses in V2, 26 in C2, 22 in V3, 23 in V4C4, and 7 in gp41
- Epitopes hotspots tended to be proximal to heavily glycosylated regions of the Env sequence, in exposed, non-helical strands of the protein – the non-uniform localization may be influenced by differential antigen processing and the glycosylation site proximity may allow binding to lectins and promote trafficking through processing pathways

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gp160(210–223) gp120(215–228) FEPIPIHYCAFPGF Vaccine murine(H-2^{bxk}) [Sastry1991]

Vaccine: *Vector/type:* peptide

- Peptides induced T-cell proliferative response to immunizing peptide and to gp160

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gp160(212–231) gp120(221–240 W6.ID) PIPIHYCAPAGFAILKC-NNK Vaccine human( ) [Jones1999]

Vaccine: *Vector/type:* recombinant protein *Strain:* W61D *HIV component:* gp120 *Stimulatory Agents:* QS21/MPL adjuvant

- An HIV seronegative volunteer was vaccinated with rgp120 and a QS21/MPL adjuvant and HIV-1 specific T-cell lines were isolated
- Two T-cell lines react specifically with this peptide

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gp160(214–220) Env( ) PIHYCAP Vaccine murine(H-2 IA^b) [Surman2001]

Vaccine: *Vector/type:* DNA, vaccinia, recombinant protein *Strain:* 1007 (clade B), UG92005 (clade D) *HIV component:* gp140 *Stimulatory Agents:* Freund's adjuvant

- This epitope is located in the C2 region of 1007 (US, clade B) and the Vβ usage of the TCR was not determined
- The epitope described here is the region of overlap of two 15 mers that were both able to stimulate IL-2 production from the hybridoma (PKVSFEPIPIHYCAP and PIHYCAPAGFAILKC)
- C57BL/6 mice were immunized with a prime-boost strategy involving three HIV-1 Env antigens: Mice were primed with DNA given i.m., 3-4 weeks later boosted with VV, and 3-4 weeks later boosted again with purified protein in Freund's adjuvant
- The vaccinia construct is a pSC11-based VV vector with the first 38 amino acids contributed by BH10 and the rest of gp120 and gp41 by the vaccine strain, the DNA construct is in the pJW4303 vector with a CMV promotor, and the purified protein is expressed from the pJW4303 vector transfected into CHO-K1 cells
- Ten days after the final boost, hybridomas were made and tested for IL-2 production using either B6 spleen cells or H-2 IA^b transfected L cells as targets and Vβ usage was determined

- Mice were immunized with an Env from either one of two clades: HIV-1 1007, a clade B strain isolated from an individual from Memphis Tennesee, and HIV-1 92UG005, a clade D strain isolated from Uganda in 1992 through the WHO
- 80 unique clonotypes were characterized from six mice
- H-2 IA^b restricted T-helper epitopes were concentrated in 5 distinct regions within the Env sequence (2 clonotype responses in V2, 26 in C2, 22 in V3, 23 in V4C4, and 7 in gp41
- Epitopes hotspots tended to be proximal to heavily glycosylated regions of the Env sequence, in exposed, non-helical strands of the protein – the non-uniform localization may be influenced by differential antigen processing and the glycosylation site proximity may allow binding to lectins and promote trafficking through processing pathways

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gp160(215–225) Env( ) IHYCAPAGFAI Vaccine murine(H-2 IA^b) [Surman2001]

Vaccine: *Vector/type:* DNA, vaccinia, recombinant protein *Strain:* 1007 (clade B), UG92005 (clade D) *HIV component:* gp140 *Stimulatory Agents:* Freund's adjuvant

- This epitope is located in the C2 region of 1007 (US, clade B) and the Vβ usage of the TCR was not determined
- The epitope described here is the region of overlap of two 15 mers that were both able to stimulate IL-2 production from the hybridoma (EPIPIHYCAPAGFAI and IHYCAPAGFAILKCN)
- C57BL/6 mice were immunized with a prime-boost strategy involving three HIV-1 Env antigens: Mice were primed with DNA given i.m., 3-4 weeks later boosted with VV, and 3-4 weeks later boosted again with purified protein in Freund's adjuvant
- The vaccinia construct is a pSC11-based VV vector with the first 38 amino acids contributed by BH10 and the rest of gp120 and gp41 by the vaccine strain, the DNA construct is in the pJW4303 vector with a CMV promotor, and the purified protein is expressed from the pJW4303 vector transfected into CHO-K1 cells
- Ten days after the final boost, hybridomas were made and tested for IL-2 production using either B6 spleen cells or H-2 IA^b transfected L cells as targets and Vβ usage was determined
- Mice were immunized with an Env from either one of two clades: HIV-1 1007, a clade B strain isolated from an individual from Memphis Tennesee, and HIV-1 92UG005, a clade D strain isolated from Uganda in 1992 through the WHO
- 80 unique clonotypes were characterized from six mice
- H-2 IA^b restricted T-helper epitopes were concentrated in 5 distinct regions within the Env sequence (2 clonotype responses in V2, 26 in C2, 22 in V3, 23 in V4C4, and 7 in gp41
- Epitopes hotspots tended to be proximal to heavily glycosylated regions of the Env sequence, in exposed, non-helical strands of the protein – the non-uniform localization may be influenced by differential antigen processing and the glycosylation site proximity may allow binding to lectins and promote trafficking through processing pathways

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gp160(216–225) Env( ) HYCAPAGFAI Vaccine murine(H-2 IA^b) [Surman2001]

Vaccine: *Vector/type:* DNA, vaccinia, recombinant protein *Strain:* 1007 (clade B), UG92005 (clade D) *HIV component:* gp140 *Stimulatory Agents:* Freund's adjuvant

- This epitope is located in the C2 region of UG92005 (UG, clade D) and Vβ usage of its TCR was not determined
- The epitope described here is the region of overlap of two 15 mers that were both able to stimulate IL-2 production from the hybridoma (EPIPIHYCAPAGFAI and HYCAPAGFAILKCND)
- C57BL/6 mice were immunized with a prime-boost strategy involving three HIV-1 Env antigens: Mice were primed with DNA given i.m., 3-4 weeks later boosted with VV, and 3-4 weeks later boosted again with purified protein in Freund's adjuvant

- The vaccinia construct is a pSC11-based VV vector with the first 38 amino acids contributed by BH10 and the rest of gp120 and gp41 by the vaccine strain, the DNA construct is in the pJW4303 vector with a CMV promotor, and the purified protein is expressed from the pJW4303 vector transfected into CHO-K1 cells
- Ten days after the final boost, hybridomas were made and tested for IL-2 production using either B6 spleen cells or H-2 IA^b transfected L cells as targets and Vβ usage was determined
- Mice were immunized with an Env from either one of two clades: HIV-1 1007, a clade B strain isolated from an individual from Memphis Tennesee, and HIV-1 92UG005, a clade D strain isolated from Uganda in 1992 through the WHO
- 80 unique clonotypes were characterized from six mice
- H-2 IA^b restricted T-helper epitopes were concentrated in 5 distinct regions within the Env sequence (2 clonotype responses in V2, 26 in C2, 22 in V3, 23 in V4C4, and 7 in gp41
- Epitopes hotspots tended to be proximal to heavily glycosylated regions of the Env sequence, in exposed, non-helical strands of the protein – the non-uniform localization may be influenced by differential antigen processing and the glycosylation site proximity may allow binding to lectins and promote trafficking through processing pathways

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gp160(220–234) gp120(225–240 SF2) PAGFAILKCNNKTFN *in vitro* stimulation ( ) [Manca1993]

- T-cell line derived from unprimed, uninfected individual
- Responds to APC pulsed with either synthetic peptide or gp120
- Human MAbs 448-D and 450-D enhance APC gp120 uptake and presentation

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gp160(220–235) gp120( ) PAGFAILKCNNKTFNY *in vitro* stimulation human(DR2) [Manca1995b]

- Peptide stimulation of PBMC from non-infected individuals *in vitro*
- Peptide priming does not always induce T-cells that recognize whole protein
- gp120 priming induced T-cells that recognize this peptide

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gp160(220–235) gp120(220–235 HXB2) PAGFAILKCNNKTFNY *in vitro* stimulation human(DR2) [Guzman1998]

- *Listeria monocytogenes*, an intracellular pathogen which is ingested by macrophages and can escape from the phagosome to replicate in the cytoplasm, was used successfully as carrier to deliver this gp120 epitope to CD4+ T-cells

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gp160(220–235) gp120(191–205 HXB2) PAGFAILKCNNKTFNY *in vitro* stimulation human(DR2) [Fenoglio1999]

- gp120 pep24 epitope exhibited antagonistic activity against proliferation of gp120-specific T-cells when flanked by unrelated amino acid sequence
- The glutathione S-transferase (GST)-peptide system can be used to display peptides; antigenicity was maintained when this peptide was expressed at the C-term end, but antagonism resulted when this peptide was expressed at the N-term end

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gp160(223–231)	gp120(238–246 HXB2)	FAILKCNNK	*in vitro* stimulation	human( )	[LiPira1998]

- Clonal heterogeneity was broad for a recall response to tetanus toxoid or PPD, but oligoclonal to primary HIV antigens, dominated in this case by TCR Vβ 22 usage
- Donor of PBMC that recognized this epitope had HLA-DR alleles 2 and 6
- The only (detected) immunogenic variant of this epitope was derived from strain NOF (YAILKCNNK)

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gp160(223–231)	gp120(194–202 HXB2)	FAILKCNNK	*in vitro* stimulation	human(DR2,6)	[Manca1996]

- Epitope was the minimal stimulatory sequence defined for two Th lines stimulated *in vitro*
- One Th line was stimulated by gp120, one by a Glutathione-S-transferase (GST)-peptide fusion
- Alanine substitutions at position 914, 196, and 202 abrogated activity for the GST-peptide stimulated line, but not for a gp120 stimulated line
- Constructs combining GST and the PAGFAILKCNNKTFNY gp120 peptide at the C-term end of GST stimulated Th cells but not at the N-term end

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gp160(223–231)	gp120(194–202 HXB2)	FAILKCNNK	*in vitro* stimulation	human(DR2,6)	[Manca1996]

- Epitope was the minimal stimulatory sequence defined for two Th lines stimulated *in vitro*
- One Th line was stimulated by p66, one by a Glutathione-S-transferase (GST)-peptide fusion protein
- Alanine substitutions at position 914, 196, and 202 abrogated activity for the GST-peptide stimulated line, but not for a gp120 stimulated line
- Constructs linking GST to the PAGFAILKCNNKTFNY gp120 peptide at the C-term end of GST stimulated Th cells, constructs linking at the N-term end did not
- The C and N termini of GST are not intrinsically permissive or non-permissive, presentation is epitope specific (see SSTVNDIQKLV for contrast)

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gp160(223–231)	gp120(237–245 SF2 HXB2)	FAILKCNNK		murine BALB/c(H-2^d)	[Fenoglio2000a]

- This peptide is an immunodominant Th epitope in BALB/c mice
- Substitutions in positions 237, 241, 243, 244 with Ala all cause reduced recognition
- Most natural analogs they tested did not cross-react, including peptides based on clade A, B, C, D, E and O sequences
- Position 237 and 244 when substituted with Ala cause an antagonistic response and the natural analogues of this epitope to loose antigenicity
- Some of the naturally occurring variants also cause an antagonistic response

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gp160(230–245)	gp120( )	NKTFNGKGPCTNVSTY	*in vitro* stimulation	human( )	[Manca1995b]

- Peptide stimulation of PBMC from non-infected individuals *in vitro*
- Peptide priming does not always induce T-cells that recognize whole protein

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gp160(235–247)	gp120(240–252)	GTGPCTNVSTVQC	Vaccine	Rhesus macaque( )	[Nehete1993]

Vaccine: *Vector/type:* peptide

- Synthetic peptide derived from conserved region of the HIV-1 envelope that stimulates a proliferative response in mice
- Proliferative response to this peptide was observed in 1/3 immunized rhesus monkeys, with a weak transient response in the other two

gp160(240–255)	gp120( )	TNVSTVQCTHGRPIY	*in vitro* stimulation	human( )	[Manca1995b]

- Peptide stimulation of PBMC from non-infected individuals *in vitro*

gp160(242–261)	gp120(242–261 IIIB)	VSTVQCTHGIRPVVST-QLLL	SHIV infection	Rhesus macaque(DRB1*0406)	[Lekutis1997b]

- A novel C2 region Th epitope was described in SHIV-89.6 infected Macaca mulatta

gp160(250–265)	gp120( )	GIRPIVSTQLLLNGSC	*in vitro* stimulation	human( )	[Manca1995b]

- Peptide stimulation of PBMC from non-infected individuals *in vitro*
- Peptide priming does not always induce T-cells that recognize whole protein

gp160(264–287)	gp120(269–292 NL43)	SLAEEEVVIRSANFTD-NAKTIIVQ	Vaccine	human( )	[Sitz1999]

Vaccine: *Vector/type:* recombinant protein *Strain:* NL43 *HIV component:* gp120, gp160

- There was a great breadth of proliferative response to Env peptides in 19 HIV-1 infected rgp160 and 17 HIV-1 infected rgp120 vaccine recipients
- 50% of vaccinees had a stimulation index of greater than 5 to this peptide

gp160(269–283)	gp120(269–283 IIIB B10)	EVVIRSANFTDNAKT	HIV-1 infection	human( )	[Wahren1989, Wahren1989a]

- 12 gag and 18 env T-cell sites were identified that could commonly evoke T-cell responses

gp160(270–285)	gp120( )	VVIRSDNFTNNAKTIC	*in vitro* stimulation	human( )	[Manca1995b]

- Peptide stimulation of PBMC from non-infected individuals *in vitro*
- Peptide priming does not always induce T-cells that recognize whole protein

gp160(274–288)	gp120(274–288 IIIB B10)	SANFTDNAKTIIVQL	HIV-1 infection	human( )	[Wahren1989, Wahren1989a]

- 12 gag and 18 env T-cell sites were identified that could commonly evoke T-cell responses

gp160(280–296)	gp120( )	NAKTIIVQLNESVAIC	*in vitro* stimulation	human( )	[Manca1995b]

- Peptide stimulation of PBMC from non-infected individuals *in vitro*
- Peptide priming does not always induce T-cells that recognize whole protein

gp160(289–297)	gp120(292–300 SF2)	NESVAINCT	Vaccine	human( )	[Botarelli1991]

Vaccine: *Vector/type:* recombinant protein *Strain:* SF2 *HIV component:* gp120

- A non-glycosylated form of SF2 gp120, env 2-3, was used as an immunogen – 20% of T-cell clones do not recognize the glycosylated form

gp160(290–306)	gp120(296–312 LAI)	SVVEINCTRPNNNTRK-S	HIV-1 infection	human( )	[Schrier1989]

- Stimulates T-cell proliferation in HIV-infected donors

gp160(296–314)	gp120(303–321 IIIB)	CTRPNNNTRKSIRIQR-GPG(Y)	Vaccine	goat( )	[Palker1989]

Vaccine: *Vector/type:* peptide *Strain:* IIIB

- Goats were immunized with peptides containing V3 type-specific neutralizing determinants coupled to T1

gp160(297–321)	gp120(302–324 MN)	TRPNYNKRKRIHIGPG-RAFYTTK	Vaccine	murine BALB/c(H-2^d)	[Oscherwitz1999a]

Vaccine: *Vector/type:* peptide *Strain:* MN *HIV component:* V3

- Epitope presented as a tandem repeat (eight copies) elicits stronger B-cell and T-cell responses than the epitope presented as a single copy
- This study indicates that the increased response was not due to neodeterminants created at the junction of the peptides, but rather due to an epitope density effect, increased immunogenicity through a high ratio of epitope to protein

gp160(297–330)	Env(303–335 BX08)	TRPNNNTRKSIHIGPG-RAFYATGEIIGDIRQAH	Vaccine	human( )	[Gahery-Segard2000a]

Vaccine: *Vector/type:* lipopeptide

- Anti-HIV lipopeptide vaccine consisting of six long peptides derived from Nef, Gag and Env HIV-1 proteins modified by a palmitoyl chain was administered in a phase I trial
- A CD4+ T-cell proliferative response to at least one of the six peptides was observed in 9/10 vaccinees – 6/10 reacted to this peptide
- 9/12 tested mounted a CTL responses to at least one of the six peptides, each of the six peptides elicited a CTL response in at least one individual – this peptide was particularly immunogenic, eliciting a CTL response in five vaccinees
- None of the 12 tested had an IgG response to gp120 or gp160 and vaccinees could be differentiated from HIV-1 seropositive individuals with a commercial HIV detection kit – no neutralizing antibodies were observed

gp160(298–307)	Env( )	RPYNNTRKGI	Vaccine	murine(H-2 IA^b)	[Surman2001]

Vaccine: *Vector/type:* DNA, vaccinia, recombinant protein *Strain:* 1007 (clade B), UG92005 (clade D) *HIV component:* gp140 *Stimulatory Agents:* Freund's adjuvant

- This epitope is located in the V3 region of UG92005 (UG, clade D) and was recognized by a hybridoma with Vβ usage not determined
- The epitope described here is the region of overlap of two 15 mers that were both able to stimulate IL-2 production from the hybridoma (TINCTRPYNNTRKGI and RPYNNTRKGIHIGPG)

- C57BL/6 mice were immunized with a prime-boost strategy involving three HIV-1 Env antigens: Mice were primed with DNA given i.m., 3-4 weeks later boosted with VV, and 3-4 weeks later boosted again with purified protein in Freund's adjuvant
- The vaccinia construct is a pSC11-based VV vector with the first 38 amino acids contributed by BH10 and the rest of gp120 and gp41 by the vaccine strain, the DNA construct is in the pJW4303 vector with a CMV promotor, and the purified protein is expressed from the pJW4303 vector transfected into CHO-K1 cells
- Ten days after the final boost, hybridomas were made and tested for IL-2 production using either B6 spleen cells or H-2 IA^b transfected L cells as targets and Vβ usage was determined
- Mice were immunized with an Env from either one of two clades: HIV-1 1007, a clade B strain isolated from an individual from Memphis Tennesee, and HIV-1 92UG005, a clade D strain isolated from Uganda in 1992 through the WHO
- 80 unique clonotypes were characterized from six mice
- H-2 IA^b restricted T-helper epitopes were concentrated in 5 distinct regions within the Env sequence (2 clonotype responses in V2, 26 in C2, 22 in V3, 23 in V4C4, and 7 in gp41
- Epitopes hotspots tended to be proximal to heavily glycosylated regions of the Env sequence, in exposed, non-helical strands of the protein – the non-uniform localization may be influenced by differential antigen processing and the glycosylation site proximity may allow binding to lectins and promote trafficking through processing pathways

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gp160(301–325) gp120( ) NNTRKSIRIQRGPGRA-FVTIGKIGN Vaccine murine( ) [Sasaki1998a]

Vaccine: *Vector/type:* DNA *Strain:* IIIB *HIV component:* Env, Rev *Stimulatory Agents:* QS-21 adjuvant

- The env response is what is being sought, but co-expression of rev is required
- Intramuscular versus nasal vaccination with DNA vaccine with a QS-21 adjuvant was studied
- QS-21 enhanced the IgG2a response mediated via Th1 cytokines IFNγ and IL-2 and delayed type hypersensitivity (DTH) in response to the V3 peptide was measured by a foot pad swelling test [Sasaki1998a]

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gp160(302–315) gp120(307–322 IIIB) NTRKSIRIQRGPGR Vaccine murine( ) [Goodman-Snitkoff1990]

Vaccine: *Vector/type:* peptide *Strain:* IIIB *HIV component:* V3

- Identification of putative Th epitopes that can stimulate an antibody response in peptide-immunized mice

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gp160(305–321) gp120(312–329) (CG)KSIRIQRGPGRAF-VTIG HIV-1 infection human( ) [Adams1997]

- Used as positive control in study examining T-cell response to four p24 Gag peptides

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gp160(308–319) gp120( ) (CKR)KIHIGPGQAFYT HIV-1 infection murine(H-$2^{b,d,k,s}$) [Ahluwalia1997b]

- A V3 loop peptide modified to resemble an Indian form (GPGQ) was incorporated into ISCOMS (immune stimulating complexes) or liposomes, and used to immunize mice – the IgG2a/IgG2b Ab response was enhanced by the presentation in the ISCOM suggestive of a Th1 response

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gp160(308–321) gp120( ) RIHIGPGRAFYTTK Vaccine murine(H-2^d) [Klinman1995]

Vaccine: *Vector/type:* peptide *Strain:* MN *HIV component:* V3

- Epitope name: SP10. Hybrid T1-V3 peptide activates IL-4 and IL-6 in a dose dependent manner
- 10-mer from V3 contributes to this response

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gp160(308–322) gp120(308–322 IIIB) RIHIGPGRAFYTTKN human( ) [Furci1997]

- 9/11 exposed-uninfected individuals in this study had a proliferative response to a C5 peptide, but only 1/11 exposed-uninfected individuals recognized this peptide
- 1/18 unexposed-uninfected controls could recognize this peptide
- Erroneously documented as IIIB sequence - most likely MN peptide

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gp160(308–322) gp120(315–329 IIIB) RIQRGPGRAFVTIGK Vaccine Rhesus macaque( ) [Nehete1993]

Vaccine: *Vector/type:* peptide

- Epitope name: P18. Synthetic peptide derived from conserved region of the HIV-1 envelope that stimulates a proliferative response in mice
- Despite the proliferative response to this peptide in mice and humans, no response was observed in 3 rhesus monkeys

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gp160(308–322) gp120(315–329 IIIB) RIQRGPGRAFVTIGK HIV-1 infection human( ) [Wasik1997a]

- Epitope name: P18. The breadth and intensity of the CTL response and the type of Th response was studied in seven rapidly progressing HIV-1+ infants
- IL-2 and γ IFN production from Th1 cells correlated with the CTLp frequency against HIV-1 Gag, Env, Nef and Pol
- IL-4 production from Th2 cells was inversely correlated with the CTLp frequency
- The HIV-1+ children with strong CTL responses had levels of anti-CD3 MAb induction of Th1 cells comparable to uninfected children
- The children that did not mount a good CTL response had dramatically decreased numbers of Th1 relative to Th2 cells

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gp160(308–322) gp120(315–329 IIIB) RIQRGPGRAFVTIGK HIV-1 infection human( ) [Wasik2000a]

- Epitope name: P18. Th responses measured by IL-2 responses to P18 and T1 in HIV-1 infected infants were undetectable at less than 1 month of age, and remained low in children with AIDS symptoms, but increased with age in children with slowly progressive disease
- The kinetics and intensity of the CTL activity during the first year of life was related to the child's ability to make Th1 responses

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gp160(308–322) gp120(315–329 IIIB) RIQRGPGRAFVTIGK HIV-1 exposed seronegative human( ) [Pinto1995a]

- Epitope name: P18. CTL activity analyzed in parallel with Th reactivity in exposed but uninfected health care workers

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gp160(308–322) gp120(315–329 MN) RIHIGPGRAFYTTKN HIV-1 exposed seronegative human( ) [Pinto1995a]

- Epitope name: P18. CTL activity analyzed in parallel with Th reactivity in exposed but uninfected health care workers

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gp160(308–322) gp120(315–329 IIIB) RIQRGPGRAFVTIGK HIV-1 infection human( ) [Clerici1989]

- Epitope name: P18. IL-2 production detection of Th lymphocytes from asymptomatic HIV-positive individuals

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gp160(308–322) gp120(315–329 IIIB) RIQRGPGRAFVTIGK HIV-1 infection human( ) [Clerici1991a]

- Epitope name: P18. Peptides stimulate Th cell function and CTL activity in similar patient populations

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gp160(308–322)	gp120(315–329 IIIB)	RIQRGPGRAFVTIGK	Vaccine	human( )	[Clerici1991b]

Vaccine: *Vector/type:* recombinant protein *Strain:* IIIB *HIV component:* gp160

- Epitope name: P18. Immunizing uninfected individuals with rgp160 results in stronger Th response than does natural infection

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gp160(308–322)	gp120(315–329 IIIB)	RIQRGPGRAFVTIGK		human( )	[Clerici1992]

- Epitope name: P18. Cell-mediated immune response to HIV-1 peptides in HIV-1 exposed seronegative men

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gp160(308–322)	gp120(315–329 IIIB)	RIQRGPGRAFVTIGK	HIV-1 infection	human( )	[Clerici1997]

- Epitope name: P18. used in a study of the influence of pentoxifylline on HIV specific T-cells

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gp160(308–322)	gp120( )	RIHIGPGRAFYTTKN		human( )	[Clerici1992]

- Epitope P18 MN: Cell-mediated immune response to HIV-1 peptides in HIV-1 exposed seronegative men

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gp160(308–322)	gp160(315–329 IIIB)	RIQRGPGRAFVTIGK	HIV-1 exposed seronegative, HIV-1 infection	human( )	[Wasik1999a]

- Epitope name: P18. IL-2 responses associated with β-chemokine expression were detectable at birth in the majority of uninfected infants born to HIV+ mothers, declining by age 6 months
- In both uninfected and infected infants of HIV-positive mothers, responses to the T1 peptide (KQIINMWQEVGKAMYA) were more frequent than responses to P18
- T1 is a highly conserved epitope, whereas P18 has a higher mutation rate due to its location in the immunodominant V3 loop region

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gp160(308–322)	gp120(315–329 IIIB)	RIQRGPGRAFVTIGK	HIV-1 exposed seronegative	human( )	[Kaul1999a]

- Epitope name: P18. Kenyan sex workers that remained seronegative were found to frequently have HIV-env peptide specific Th responses detected by an IL-2 assay (11/20 cases) and mucosal genital tract anti-HIV IgA (16/21 cases)
- The helper epitopes used in this study were noted to be previously described [Clerici1989], and were not explicitly described in [Kaul1999a]

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gp160(308–322)	gp120(315–329 IIIB)	RIQRGPGRAFVTIGK	HIV-1 exposed seronegative, HIV-1 infection	human( )	[Kuhn2001]

- Epitope name: P18. In a S. African perinatal transmission study, 33% (33/86) of cord blood samples from infants with seropositive mothers produced T-helper responses (measured by a bioassay measuring IL-2 production in a murine cell line and confirmed with a proliferation assay) against a peptide cocktail containing Th epitopes P18 MN, P18 IIIB, T1, T2, and TH4
- The mothers were predominantly infected subtype C but the T-helper response was detectable in a number of cord blood samples despite using peptides based on B subtype reagents
- 3/33 infants with cord blood T-helper responses to Env were infected *in utero*, 2/33 were lost to follow up, and 28/33 were not infected – 6/53 of the infants with cord blood that was unresponsive to Env peptide stimulation were infected before delivery, and 8/47 contracted HIV intrapartum or via breast-feeding
- Measurable HIV specific T-helper responses elicited in the immunologically immature newborn, possibly in response to *in utero* exposure, are associated with a protective natural immunity that helps block mother-infant transmission of HIV-1

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gp160(308–322)	gp120(315–329 MN)	RIHIGPGRAFYTTKN	HIV-1 exposed seronegative, HIV-1 infection	human( )	[Kuhn2001]

- Epitope name: P18. In a S. African perinatal transmission study, 33% (33/86) of cord blood samples from infants with seropositive mothers produced T-helper responses (measured by a bioassay measuring IL-2 production in a murine cell line and confirmed with a proliferation assay) against a peptide cocktail containing Th epitopes P18 MN, P18 IIIB, T1, T2, and TH4
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- Measurable HIV specific T-helper responses elicited in the immunologically immature newborn, possibly in response to *in utero* exposure, are associated with a protective natural immunity that helps block mother-infant transmission of HIV-1

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gp160(308–322)	gp120(315–329 IIIB)	RIQRGPGRAFVTIGK	HIV-1 infection	human(DR)	[Baier1995]

- Epitope name: P18. Linked HIV-1 T1 and P18 peptides to anti-HLA-DR and IgD Fab fragments to enhance uptake by antigen presenting cells thus increase immunogenicity

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gp160(308–322)	gp120(315–329 IIIB)	RIQRGPGRAFVTIGK	Vaccine	murine(H-2 A^d)	[Takahashi1990]

Vaccine: *Vector/type:* vaccinia *Strain:* IIIB *HIV component:* gp160

- Epitope name: P18. Induces both class II restricted CD4+ Th cells, and class I restricted CD8+ CTL

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gp160(308–322)	gp120(315–329 IIIB)	RIQRGPGRAFVTIGK	Peptide-HLA interaction	murine(H-2 I-A^d)	[Takeshita1995a]

- Epitope name: P18. Binds Class II H-2 I-A^d requiring riqrgPgRaFvti, and Class I H-2 D^d, requiring iGPgRaFvtI

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gp160(308–322)	Env( )	RIQRGPRAFVTIGK	Vaccine	murine(H-2^d)	[Lu1999a]

Vaccine: *Vector/type:* DNA, CMV promotor *Strain:* IIIB *HIV component:* gp160, Rev *Stimulatory Agents:* MIP-1α expression vector

- Epitope name: P18. MIP-1α expression plasmid co-inoculated with a DNA vaccine consisting of HIV-1 pCMV160IIIB and pcRev enhanced the HIV-specific T-cell immune response as measured by a CTL test against using V3 peptide pulsed targets, and a DTH test to V3 peptide.
- The IgG1/IgG2a response was lowered with co-inoculation of MIP-1α, suggesting it preferentially elicits a Th1 response

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gp160(308–327)	gp120(306–325 MN)	RIHIGPGRAFYTTKNII-GIT	HIV-1 infection	human(DRB1*0101)	[Hayball1997]

- Tandem repeated presentation of epitope enhances binding to class II molecule and therefore induction of T-cell proliferation
- Tandem peptides are thought to enhance proliferation through improved recruiting of CD4 to the activation complex, which can counter-balance gp120's sequestering of CD4 and consequential inhibition of a proliferative response

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gp160(309–323)	gp120(309–323 IIIB B10)	EQRGPGRAFVTIGKI	HIV-1 infection	human( )	[Wahren1989, Wahren1989a]

- 12 gag and 18 env T-cell sites were identified that could commonly evoke T-cell responses

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gp160(309–325) gp120(314–330) IQRGPGRAFVTIGKIGN HIV-1 infection human( ) [Caruso1997]

- As HIV-1-infected individuals progress to disease, T-cells show reduced ability to proliferate in response to HIV antigen, but retain the ability to express the activation antigens CD25 and CD71
- The ability to express activation markers in response to HIV is retained, but the response to tetanus toxoid recall antigen is lost
- This study investigated CD25 and CD71 expression in PBMC from patients at various stages of progression, measuring the response to *in vitro* stimulation by peptide cocktail containing four antigenic Env peptides, or p17 and p24

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gp160(311–320) gp120( ) RGPGPAFVTI Vaccine murine(H-2^d) [Xin1998]

Vaccine: *Vector/type:* DNA, CMV promotor *Strain:* IIIB *HIV component:* gp160, Rev *Stimulatory Agents:* IL-2 expression vector

- Intranasal immunization with IL-2 expression plasmid in addition to DNA vaccine amplifies cellular response to antigen, probably via activation of Th type 1 (Th1) cells

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gp160(311–320) gp120( ) RGPGPAFVTI Vaccine murine(H-2^d) [Xin1999a]

Vaccine: *Vector/type:* DNA, CMV promotor *Strain:* IIIB *HIV component:* gp160, Rev *Stimulatory Agents:* IL-15 expression vector

- Intranasal immunization with IL-15 expression plasmid in addition to DNA vaccine increases DTH response and CTL activity to the antigen, and decreases the serum IgG1 to IgG2a ratio, enhancing Th type 1 (Th1) cell-mediated immunity
- Expression of IL-2 or IL-15 can enhance Th1 response to the vaccine, but they to do not appear to elicit a synergistic response

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gp160(311–320) gp120( ) RGPGPAFVTI Vaccine murine(H-2^d) [Ihata1999a]

Vaccine: *Vector/type:* DNA, CMV promotor *Strain:* IIIB *HIV component:* gp160, Rev *Stimulatory Agents:* CD40L expression vector

- CD40L expression increases DTH, and Th1-dependent responses based on enhanced IgG2a titers, with no lowering of IgG1 titers
- Elispot assay indicated co-injection with hCD40L resulted in greater numbers of IFN-γ producing Th1cells, as well as increased IL-4 producing Th2 cells
- Results suggest hCD40L enhances both Th1 and Th2 cells, and such a pattern of induction is unique among adjuvants, as most adjuvants increase either Th1 or Th2

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gp160(311–322) Env( ) RGPGRAFVTIGK Vaccine murine(H-2^d) [Kusakabe2000]

Vaccine: *Vector/type:* DNA, CMV promotor *Strain:* IIIB *HIV component:* gp160, Rev *Stimulatory Agents:* pGM-CSF expression vector

- The timing of delivery of the pGM-CSF expression plasmid for intramuscular DNA pCMV160IIIB/Rev vaccination impacts the Th response, maximizing Th2 responses when administered 3 days prior to the DNA vaccine, and Th1 responses when administered 3 days after the DNA vaccine

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gp160(314–328)	gp120(314–328 IIIB B10)	GRAFVTIGKIGNMRQ	HIV-1 infection	human( )	[Wahren1989, Wahren1989a]

- 12 gag and 18 env T-cell sites were identified that could commonly evoke T-cell responses

gp160(314–341)	gp120(319–346 NL43)	GRAFVTIGKIGNMRQ-AHCNISRAKWNAT	Vaccine	human( )	[Sitz1999]

Vaccine: *Vector/type:* recombinant protein *Strain:* NL43 *HIV component:* gp120, gp160

- There was a great breadth of proliferative response to Env peptides in 19 HIV-1 infected rgp160 and 17 HIV-1 infected rgp120 vaccine recipients
- More than 25% of vaccinees had a stimulation index of greater than 5 to this peptide

gp160(315–328)	Env( )	RAYYTTNIVGNIRQ	Vaccine	murine(H-2 IA^b)	[Surman2001]

Vaccine: *Vector/type:* DNA, vaccinia, recombinant protein *Strain:* 1007 (clade B), UG92005 (clade D) *HIV component:* gp140 *Stimulatory Agents:* Freund's adjuvant

- This epitope is located in the V3 region of UG92005 (UG, clade D) and was recognized by two hybridomas with Vβ usage not determined, but one used Vα 8
- C57BL/6 mice were immunized with a prime-boost strategy involving three HIV-1 Env antigens: Mice were primed with DNA given i.m., 3-4 weeks later boosted with VV, and 3-4 weeks later boosted again with purified protein in Freund's adjuvant
- The vaccinia construct is a pSC11-based VV vector with the first 38 amino acids contributed by BH10 and the rest of gp120 and gp41 by the vaccine strain, the DNA construct is in the pJW4303 vector with a CMV promotor, and the purified protein is expressed from the pJW4303 vector transfected into CHO-K1 cells
- Ten days after the final boost, hybridomas were made and tested for IL-2 production using either B6 spleen cells or H-2 IA^b transfected L cells as targets and Vβ usage was determined
- Mice were immunized with an Env from either one of two clades: HIV-1 1007, a clade B strain isolated from an individual from Memphis Tennesee, and HIV-1 92UG005, a clade D strain isolated from Uganda in 1992 through the WHO
- 80 unique clonotypes were characterized from six mice
- H-2 IA^b restricted T-helper epitopes were concentrated in 5 distinct regions within the Env sequence (2 clonotype responses in V2, 26 in C2, 22 in V3, 23 in V4C4, and 7 in gp41
- Epitopes hotspots tended to be proximal to heavily glycosylated regions of the Env sequence, in exposed, non-helical strands of the protein – the non-uniform localization may be influenced by differential antigen processing and the glycosylation site proximity may allow binding to lectins and promote trafficking through processing pathways

gp160(317–331)	gp160(324–338 IIIB)	FVTIGKIGNMRQAHC	Vaccine	murine(H-2^k, H-2^d)	[Berzofsky1991, Berzofsky1991a]

Vaccine: *Vector/type:* recombinant protein *Strain:* IIIB *HIV component:* gp160 *Stimulatory Agents:* Freund's adjuvant

- B10.BR (H-$2A^k$, E^k) and B10.D2 (H-$2A^d$, E^d) mice immunized with rec gp160 showed a proliferative response to this peptide
- FVTIGKIGNMRQAHCNISRAKWNNTLKQIDSKL encompasses several murine Th epitopes including FVTIGKIGNMRQAHC and is referred to as a "multideterminant region" or cluster peptide

gp160(317–331)	gp120(324–338 IIIB)	FVTIGKIGNMRQAHC	Vaccine	murine(H-$2^{k,d}$)	[Hale1989]

Vaccine: *Strain:* IIIB *HIV component:* gp160

- Six multideterminant helper T-cell regions are recognized by mice of three or four MHC types

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gp160(317–349)	gp160(324–356 IIIB)	FVTIGKIGNMRQAHC-NISRAKWNNTLKQIDS-KL	HIV-1 infection, Vaccine	human, murine(H-2^k, H-2^d)	[Berzofsky1991, Berzofsky1991a]

Vaccine: *Vector/type:* recombinant protein *Strain:* IIIB *HIV component:* gp160 *Stimulatory Agents:* Freund's adjuvant

- FVTIGKIGNMRQAHCNISRAKWNNTLKQIDSKL encompasses several murine Th epitopes and is referred to as a "multideterminant region" or cluster peptide
- Six multideterminant region cluster peptides were evaluated Th responses in different MHC/HLA backgrounds after vaccination of mice with gp160, or in infected people
- This cluster peptide elicited proliferative responses in cells from B10.BR mice (H-2A^k, E^k) and B10.D2 mice (H-2A^d, E^d), but shorter peptides from within this region stimulated H-2^k, H-2^d, H-2^b and H-2^s responses
- IL-2 production in response to this peptide was observed in 58% (21/36) of asymptomatic HIV-infected individuals

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gp160(319–338)	gp120(320–339 89.6)	RRNIIGDIRQAHCNISR-AKW	Vaccine	murine(H-2^k, H-2^d)	[Dai2001]

Vaccine: *Vector/type:* recombinant protein *Strain:* 89.6 *HIV component:* gp120 *Stimulatory Agents:* mutant R192G heat-labile toxin from *E. coli* as adjuvant

- Promiscuous immunodominant epitope in gp120 were mapped by overlapping peptides in CBA/J H-2^k and BALB/c H-2^d mice, and all were found to be in the outer domain, proximal to regions of structural disorder indicated by the crystal structure or by sequence divergence
- This peptide was recognized by 7/10 CBA/J and 7/10 BALB/c mice with SI $>$ 4, averaging 6.3 and 4.8, and is considered to be promiscuously immunodominant
- Uniquely immunodominant sequences tended to be in the interior of the protein

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gp160(321–336)	gp120( )	RIIGDIRKAHCNISRY	*in vitro* stimulation	human( )	[Manca1995b]

- Peptide stimulation of PBMC from non-infected individuals *in vitro*
- Peptide priming does not always induce T-cells that recognize whole protein

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gp160(322–336)	Env( )	IIGDIRQAHCNISRE	Vaccine	murine(H-2 IA^b)	[Surman2001]

Vaccine: *Vector/type:* DNA, vaccinia, recombinant protein *Strain:* 1007 (clade B), UG92005 (clade D) *HIV component:* gp140 *Stimulatory Agents:* Freund's adjuvant

- This epitope is located in the V3 region of 1007 (US, clade B) and was recognized by three hybridomas with Vβ usage Vβ 6 and not determined
- C57BL/6 mice were immunized with a prime-boost strategy involving three HIV-1 Env antigens: Mice were primed with DNA given i.m., 3-4 weeks later boosted with VV, and 3-4 weeks later boosted again with purified protein in Freund's adjuvant

- The vaccinia construct is a pSC11-based VV vector with the first 38 amino acids contributed by BH10 and the rest of gp120 and gp41 by the vaccine strain, the DNA construct is in the pJW4303 vector with a CMV promotor, and the purified protein is expressed from the pJW4303 vector transfected into CHO-K1 cells
- Ten days after the final boost, hybridomas were made and tested for IL-2 production using either B6 spleen cells or H-2 IA^b transfected L cells as targets and Vβ usage was determined
- Mice were immunized with an Env from either one of two clades: HIV-1 1007, a clade B strain isolated from an individual from Memphis Tennesee, and HIV-1 92UG005, a clade D strain isolated from Uganda in 1992 through the WHO
- 80 unique clonotypes were characterized from six mice
- H-2 IA^b restricted T-helper epitopes were concentrated in 5 distinct regions within the Env sequence (2 clonotype responses in V2, 26 in C2, 22 in V3, 23 in V4C4, and 7 in gp41
- Epitopes hotspots tended to be proximal to heavily glycosylated regions of the Env sequence, in exposed, non-helical strands of the protein – the non-uniform localization may be influenced by differential antigen processing and the glycosylation site proximity may allow binding to lectins and promote trafficking through processing pathways

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gp160(322–336) Env( ) IVGNIRQAHCNVSKA Vaccine murine(H-2 IA^b) [Surman2001]

Vaccine: *Vector/type:* DNA, vaccinia, recombinant protein *Strain:* 1007 (clade B), UG92005 (clade D) *HIV component:* gp140 *Stimulatory Agents:* Freund's adjuvant

- This epitope is located in the V3 region of UG92005 (UG, clade D) and was recognized by three hybridomas with Vβ usage Vβ 6, 8.1, and not determined
- C57BL/6 mice were immunized with a prime-boost strategy involving three HIV-1 Env antigens: Mice were primed with DNA given i.m., 3-4 weeks later boosted with VV, and 3-4 weeks later boosted again with purified protein in Freund's adjuvant
- The vaccinia construct is a pSC11-based VV vector with the first 38 amino acids contributed by BH10 and the rest of gp120 and gp41 by the vaccine strain, the DNA construct is in the pJW4303 vector with a CMV promotor, and the purified protein is expressed from the pJW4303 vector transfected into CHO-K1 cells
- Ten days after the final boost, hybridomas were made and tested for IL-2 production using either B6 spleen cells or H-2 IA^b transfected L cells as targets and Vβ usage was determined
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- Epitope hotspots tended to be proximal to heavily glycosylated regions of the Env sequence, in exposed, non-helical strands of the protein – the non-uniform localization may be influenced by differential antigen processing and the glycosylation site proximity may allow binding to lectins and promote trafficking through processing pathways

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gp160(324–336) Env( ) GNIRQAHCNVSKA Vaccine murine(H-2 IA^b) [Surman2001]

Vaccine: *Vector/type:* DNA, vaccinia, recombinant protein *Strain:* 1007 (clade B), UG92005 (clade D) *HIV component:* gp140 *Stimulatory Agents:* Freund's adjuvant

- This epitope is located in the V3 region of UG92005 (UG, clade D) and was recognized by two hybridoma with Vβ usage Vβ8.2 and not determined

- The epitope described here is the region of overlap of two 15 mers that were both able to stimulate IL-2 production from the hybridoma (IVGNIRQAHCNVSKA and GNIRQAHCNVSKAKW)
- C57BL/6 mice were immunized with a prime-boost strategy involving three HIV-1 Env antigens: Mice were primed with DNA given i.m., 3-4 weeks later boosted with VV, and 3-4 weeks later boosted again with purified protein in Freund's adjuvant
- The vaccinia construct is a pSC11-based VV vector with the first 38 amino acids contributed by BH10 and the rest of gp120 and gp41 by the vaccine strain, the DNA construct is in the pJW4303 vector with a CMV promotor, and the purified protein is expressed from the pJW4303 vector transfected into CHO-K1 cells
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gp160(324–338) Env( ) GNIRQAHCNVSKAKW Vaccine murine(H-2 IA^b) [Surman2001]

Vaccine: *Vector/type:* DNA, vaccinia, recombinant protein *Strain:* 1007 (clade B), UG92005 (clade D) *HIV component:* gp140 *Stimulatory Agents:* Freund's adjuvant

- This epitope is located in the V3 region of UG92005 (UG, clade D) and was recognized by eleven hybridomas with Vβ usage Vβ5, 7, 8.1, 8.2, 11 and not determined – a Vβ 8.1's and Vβ 8.2 also were shown to use Vα 8, and one of the ND used Vα 2
- C57BL/6 mice were immunized with a prime-boost strategy involving three HIV-1 Env antigens: Mice were primed with DNA given i.m., 3-4 weeks later boosted with VV, and 3-4 weeks later boosted again with purified protein in Freund's adjuvant
- The vaccinia construct is a pSC11-based VV vector with the first 38 amino acids contributed by BH10 and the rest of gp120 and gp41 by the vaccine strain, the DNA construct is in the pJW4303 vector with a CMV promotor, and the purified protein is expressed from the pJW4303 vector transfected into CHO-K1 cells
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- Mice were immunized with an Env from either one of two clades: HIV-1 1007, a clade B strain isolated from an individual from Memphis Tennesee, and HIV-1 92UG005, a clade D strain isolated from Uganda in 1992 through the WHO
- 80 unique clonotypes were characterized from six mice
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- Epitopes hotspots tended to be proximal to heavily glycosylated regions of the Env sequence, in exposed, non-helical strands of the protein – the non-uniform localization may be influenced by differential antigen processing and the glycosylation site proximity may allow binding to lectins and promote trafficking through processing pathways

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gp160(327–341)	gp120(327–341 HXB2)	RQAHCNISRAKWNNT	Vaccine	murine(I-A^d)	[Warren1992]

Vaccine: *Vector/type:* recombinant protein *Strain:* HXB2 *HIV component:* gp120

- Minimum epitope and MHC restriction determined for CTL clone that recognizes the N-terminal flank of the V3 loop

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gp160(331–345)	gp120( )	CNISRAQWNNTLEQI	*in vitro* stimulation	human( )	[Manca1995b]

- Peptide stimulation of PBMC from non-infected individuals *in vitro*
- Peptide priming does not always induce T-cells that recognize whole protein

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gp160(332–354)	gp120(337–359 NL43)	NISRAKWNATLKQIAS-KLREQFG	Vaccine, HIV-1 infection	human( )	[Sitz1999]

Vaccine: *Vector/type:* recombinant protein *Strain:* NL43 *HIV component:* gp120, gp160

- There was a great breadth of proliferative response to Env peptides in 19 HIV-1 infected rgp160 and 17 HIV-1 infected rgp120 vaccine recipients
- More than 30% of vaccinees had a stimulation index of greater than 5 to this peptide

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gp160(335–349)	gp160(342–356 IIIB)	RAKWNNTLKQIDSKL	Vaccine	murine(H-2^k, H-2^b, H-2^s)	[Berzofsky1991, Berzofsky1991a]

Vaccine: *Vector/type:* recombinant protein *Strain:* IIIB *HIV component:* gp160 *Stimulatory Agents:* Freund's adjuvant

- B10.BR (H-2A^k, E^k), B10.A(5R) (H-2A^b, E^b) and B10.S(9R) (H-2A^s, E^s) mice immunized with rec gp160 showed a proliferative response to this peptide
- FVTIGKIGNMRQAHCNISRAKWNNTLKQIDSKL encompasses several murine Th epitopes including RAKWNNTLKQIDSKL and is referred to as a "multideterminant region" or cluster peptide

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gp160(335–349)	gp120(342–356 IIIB)	RAKWNNTLKQICSKL	Vaccine	murine(H-2^{k,t4,i5})	[Hale1989]

Vaccine: *Strain:* IIIB *HIV component:* gp160

- Six multideterminant helper T-cell regions are recognized by mice of three or four MHC types

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gp160(339–359)	gp120(340–359 89.6)	NNTLQQIVIKLREKFR-NKTI	Vaccine	murine(H-2^k, H-2^d)	[Dai2001]

Vaccine: *Vector/type:* recombinant protein *Strain:* 89.6 *HIV component:* gp120 *Stimulatory Agents:* mutant R192G heat-labile toxin from *E. coli* as adjuvant

- Promiscuous immunodominant epitope in gp120 were mapped by overlapping peptides in CBA/J H-2^k and BALB/c H-2^d mice, and all were found to be in the outer domain, proximal to regions of structural disorder indicated by the crystal structure or by sequence divergence
- This peptide was recognized by 4/10 CBA/J and 6/10 BALB/c mice with SI $>$ 4, averaging 4.9 and 5.5 and is considered to be promiscuously immunodominant
- Uniquely immunodominant sequences tended to be in the interior of the protein

gp160(341–356)	gp120( )	TLEQIVKKLREQFGNC	*in vitro* stimulation	human( )	[Manca1995b]
• Peptide stimulation of PBMC from non-infected individuals *in vitro* • Peptide priming does not always induce T-cells that recognize whole protein					
gp160(344–357)	gp120(346–359)	QIVKKLREQFGNNK	HIV-1 infection	human( )	[Krowka1990]
• Conjugation of HIV peptides to liposomes and rIL-2 stimulation may enhance cell-mediated responses					
gp160(353–360)	gp120(355–362 IIIB)	FGNNKTII	SHIV infection	Rhesus macaque( )	[Lekutis1997b]
• C3 region minimal epitope determined through fine epitope mapping • Cell line was lost prior to confirmation of MHC requirements					
gp160(363–372)	gp120(368–377 LAI)	QSSGGDPEIV	HIV-1 infection	human( )	[Schrier1989]
• Stimulates T-cell proliferation in HIV-infected donors					
gp160(364–378)	gp120(364–378 IIIB B10)	SSGGKPEIVTHSFNC	HIV-1 infection	human( )	[Wahren1989, Wahren1989a]
• 12 gag and 18 env T-cell sites were identified that could commonly evoke T-cell responses					
gp160(369–383)	gp120(369–383 IIIB B10)	PEIVTHSFNCGGEFF	HIV-1 infection	human( )	[Wahren1989, Wahren1989a]
• 12 gag and 18 env T-cell sites were identified that could commonly evoke T-cell responses					
gp160(381–395)	gp120( )	EFFYCNTTQLFNNTW	*in vitro* stimulation	human( )	[Manca1995b]
• Peptide stimulation of PBMC from non-infected individuals *in vitro* • Peptide priming does not always induce T-cells that recognize whole protein					
gp160(394–408)	gp120(394–408 IIIB B10)	TWFNSTWSTKGSNNT	HIV-1 infection	human( )	[Wahren1989, Wahren1989a]
• 12 gag and 18 env T-cell sites were identified that could commonly evoke T-cell responses					
gp160(396–411)	gp120( )	FNNTWRLNHTEGTKG-C	*in vitro* stimulation	human( )	[Manca1995b]
• Peptide stimulation of PBMC from non-infected individuals *in vitro* • Peptide priming does not always induce T-cells that recognize whole protein					

gp160(399–413)	gp120(399–413 IIIB B10)	TWSTKGSNNTEGSDT	HIV-1 infection	human( )	[Wahren1989, Wahren1989a]

- 12 gag and 18 env T-cell sites were identified that could commonly evoke T-cell responses

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gp160(404–423)	gp120(400–419 89.6)	GTNGTEGNDIITLQCRIKQI	Vaccine	murine(H-2^k, H-2^d)	[Dai2001]

Vaccine: *Vector/type:* recombinant protein *Strain:* 89.6 *HIV component:* gp120 *Stimulatory Agents:* mutant R192G heat-labile toxin from *E. coli* as adjuvant

- Promiscuous immunodominant epitope in gp120 were mapped by overlapping peptides in CBA/J H-2^k and BALB/c H-2^d mice, and all were found to be in the outer domain, proximal to regions of structural disorder indicated by the crystal structure or by sequence divergence
- This peptide was recognized by 4/10 CBA/J and 6/10 BALB/c mice with SI $>$ 4, averaging 4.9 and 5.5 and is considered to be promiscuously immunodominant
- Uniquely immunodominant sequences tended to be in the interior of the protein

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gp160(410–429)	gp120(410–429 PV22)	GSDTITLPCRIKQFINMWQE	HIV-1 infection	human(DR4)	[Callahan1990]

- Synthetic peptides representing natural variants were used to test for recognition in the context DR4

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gp160(410–429)	gp120(410–429 PV22)	GSDTITLPCRIKQFINMWQE	HIV-1 infection	human(DR4(Dw10))	[Polydefkis1990]

- Human CD4+ T-cell clones lyse recombinant vaccinia virus-infected cells that synthesize envelope gp160

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gp160(416–431)	gp120( )	LPCRIKQIINMWQEVY	*in vitro* stimulation	human( )	[Manca1995b]

- Peptide stimulation of PBMC from non-infected individuals *in vitro*
- Peptide priming does not always induce T-cells that recognize whole protein

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gp160(418–436)	Env(417–435)	CRIKQIINMWQGVGKAMYA	HIV-1 infection	human, chimpanzee( )	[Nehete1998a]

- HIV-infected chimpanzees and HIV-positive patients show positive proliferative responses to multiple peptides from five conserved regions of the HIV-1 Env

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gp160(421–436)	gp120(426–441 IIIB)	KQFINMWQEWGKAMYA		human( )	[Furci1997]

- Epitope T1 variant: 9/11 exposed-uninfected individuals in this study had a proliferative response to a C5 peptide, but none reacted with this previously defined epitope
- IIIB position 435 listed as "W" in this epitope as opposed to "V" in the sequence

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gp160(421–436)	gp120(428–433 IIIB)	KQIINMWQEVGKAMYA	HIV-1 infection	human( )	[Wasik2000a]

- Epitope name: T1. Th responses measured by IL-2 responses to P18 and T1 in HIV-1 infected infants were undetectable at less than 1 month of age, and remained low in children with AIDS symptoms, but increased with age in children with slowly progressive disease
- The kinetics and intensity of the CTL activity during the first year of life was related to the child's ability to make Th1 responses

gp160(421–436) gp120(428–433 IIIB) KQIINMWQEVGKAMYA HIV-1 infection human( ) [Wasik1997a]
- Epitope name: T1. The breadth and intensity of the CTL response and the type of Th response was studied in seven rapidly progressing HIV-1+ infants
- IL-2 and γ IFN production from Th1 cells correlated with the CTLp frequency against HIV-1 Gag, Env, Nef and Pol
- IL-4 production from Th2 cells was inversely correlated with the CTLp frequency
- The HIV-1+ children with strong CTL responses had levels of anti-CD3 MAb induction of Th1 cells comparable to those of uninfected children

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gp160(421–436) gp120(428–443 IIIB) KQIINMWQEVGKAMYA Vaccine human( ) [Berzofsky1988]

Vaccine: *Vector/type:* vaccinia *Strain:* IIIB *HIV component:* gp160
- Epitope name: T1. Proliferative response to T1 and T2 peptides in 14 immunized, uninfected humans

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gp160(421–436) gp120(428–443 IIIB) KQIINMWQEVGKAMYA Vaccine goat( ) [Palker1989]

Vaccine: *Vector/type:* peptide *Strain:* IIIB
- Epitope name: T1. Goats immunized with peptides containing V3 type-specific neutralizing determinants coupled to T1

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gp160(421–436) gp120(428–443 IIIB) KQIINMWQEVGKAMYA HIV-1 infection human( ) [Clerici1989]
- Epitope name: T1. IL-2 production detection of Th lymphocytes from asymptomatic HIV-positive individuals

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gp160(421–436) gp120(428–443 IIIB) KQIINMWQEVGKAMYA HIV-1 infection human( ) [Clerici1991a]
- Epitope name: T1. Peptides stimulate Th cell function and CTL activity in similar patient populations

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gp160(421–436) gp120(428–443 IIIB) KQIINMWQEVGKAMYA Vaccine human( ) [Clerici1991b]

Vaccine: *Vector/type:* recombinant protein *Strain:* IIIB *HIV component:* gp160
- Epitope name: T1. Immunizing uninfected individuals with rgp160 results in stronger Th response than does natural infection

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gp160(421–436) gp120(428–443 IIIB) KQIINMWQEVGKAMYA HIV-1 exposed seronegative human( ) [Clerici1992]
- Epitope name: T1. Cell-mediated immune response to HIV-1 peptides in HIV-1 exposed seronegative men

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gp160(421–436) gp120(428–443 IIIB) KQIINMWQEVGKAMYA Vaccine murine( ) [Veronese1994]

Vaccine: *Vector/type:* bacteriophage coat protein *Strain:* MN *HIV component:* V3
- Epitope T1 was engineered into a filamentous bacteriophage coat protein, and the Th epitope stimulated Ab production to the V3 loop

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gp160(421–436) gp120(428–443 IIIB) KQIINMWQEVGKAMYA Vaccine chimpanzee( ) [Haynes1993]

Vaccine: *Vector/type:* peptide *Strain:* IIIB
- Epitope name: T1. Hybrid T1-V3 peptide immunogenicity reduced when the fusogenic domain of gp41 was added

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gp160(421–436)	gp120(428–443 IIIB)	KQIINMWQEVGKAMYA	HIV-1 infection	human( )	[Clerici1997]

- Epitope name: T1. Used in a study of the influence of pentoxifylline on HIV specific T-cells

gp160(421–436)	gp120(428–443 IIIB)	KQIINMWQEVGKAMYA	HIV-1 exposed seronegative	human( )	[Pinto1995a]

- Epitope name: T1. CTL activity analyzed in parallel with Th reactivity in exposed but uninfected health care workers

gp160(421–436)	gp160(428–433 IIIB)	KQIINMWQEVGKAMYA	HIV-1 exposed seronegative, HIV-1 infection	human( )	[Wasik1999a]

- Epitope name: T1. IL-2 responses associated with β-chemokine expression were detectable at birth in the majority of uninfected infants born to HIV+ mothers, declining by age 6 months
- T1 peptide: In both uninfected and infected infants of HIV-positive mothers, responses to the T1 peptide were more frequent than responses to P18 (RIQRGPGRAFVTIGK)
- T1 is a highly conserved epitope, whereas P18 has a higher mutation rate due to its location in the immunodominant V3 loop region

gp160(421–436)	gp120(428–443 IIIB)	KQIINMWQEVGKAMYA	HIV-1 infection	human( )	[Kaul1999a]

- Epitope name: T1. Kenyan sex workers that remained seronegative were found to frequently have HIV-env peptide specific Th responses detected by an IL-2 assay (11/20 cases) and mucosal genital tract anti-HIV IgA (16/21 cases)
- Helper epitopes used in this study were noted to be previously described [Clerici1989], and were not explicitly described in [Kaul1999a]

gp160(421–436)	gp120( )	KQIINMWQEVGKAMYA	HIV-1 infection, Vaccine	human( )	[Bartlett1998a]

Vaccine: *Vector/type:* peptide *Strain:* MN *HIV component:* polyepitope

- Epitope name: T1. C4-V3 PV (polyvalent HIV envelope synthetic peptide immunogen) consisted of T1 helper epitope presented in tandem with a V3 loop CTL epitope from one of four different North American strains
- This was a pilot phase I study involving vaccination of ten HIV-infected subjects who were HLA-B7-positive
- Enhanced lymphoproliferative response to peptide was observed in 5/8 vaccinees – increase in neutralizing antibody responses in 4/8 vacinees

gp160(421–436)	gp120( )	KQIINMWQEVGKAMYA	HIV-1 exposed seronegative, HIV-1 infection	human( )	[Kuhn2001]

- Epitope name: T1. In a S. African perinatal transmission study, 33% (33/86) of cord blood samples from infants with seropositive mothers produced T-helper responses (measured by a bioassay measuring IL-2 production in a murine cell line and confirmed with a proliferation assay) against a peptide cocktail containing Th epitopes P18 MN, P18 IIIB, T1, T2, and TH4
- The mothers were predominantly infected subtype C but the T-helper response was detectable in a number of cord blood samples despite using peptides based on B subtype reagents
- 3/33 infants with cord blood T-helper responses to Env were infected *in utero*, 2/33 were lost to follow up, and 28/33 were not infected – 6/53 of the infants with cord blood that was unresponsive to Env peptide stimulation were infected before delivery, and 8/47 contracted HIV intrapartum or via breast-feeding
- Measurable HIV specific T-helper responses elicited in the immunologically immature newborn, possibly in response to *in utero* exposure, are associated with a protective natural immunity that helps block mother-infant transmission of HIV-1

gp160(421–436)	gp120(428–443 IIIB)	KQIINMWQEVGKAMYA	Vaccine peptide IIIB	human(DR)	[Baier1995]

- Epitope name: T1. Linked HIV-1 T1 and P18 peptides to anti-HLA-DR and anti-IgD Fab fragments to enhance uptake by antigen presenting cells and thus increase immunogenicity

gp160(421–436)	gp120(428–443 IIIB)	KQIINMWQEVGKAMYA	Vaccine	murine(H-2$E\alpha E\beta^k$)	[Boehncke1993]

Vaccine: *Vector/type:* peptide *Strain:* IIIB

- Epitope name: T1. C3H H2^k mice were used for immunization in the study because H-2^k mice are particularly good T1 responders – T1 can be presented by $E\alpha E\beta^k$ but not $E\alpha E\beta^b$ – the nature of the T1 class II molecular interaction was thoroughly explored
- Alanine substitutions across peptide did not negatively affect MHC binding or effective presentation of epitope, except at three critical residues (432N, 435Q, 439K), however substitutions with larger side chains often diminished activity – only a few amino acids were found to be critical for class II interaction and for maintaining T-cell receptor specificity
- A gain in potency was observed when 436E was replaced with A, suggesting that substitutions in positions that interfere with binding might allow the design of a more potent vaccine

gp160(421–436)	gp120(428–443 IIIB)	KQIINMWQEVGKAMYA	Vaccine	murine(H-2^d)	[Klinman1995]

Vaccine: *Vector/type:* peptide *Strain:* IIIB

- Epitope name: T1. Hybrid T1-V3 peptide activates IL-4 and IL-6 in a dose dependent manner

gp160(421–436)	gp160(428–443 IIIB)	KQIINMWQEVGKAMYA	Vaccine	murine(H-2^k, H-2^s, H-2^d)	[Berzofsky1991, Berzofsky1991a]

Vaccine: *Vector/type:* recombinant protein *Strain:* IIIB *HIV component:* gp160 *Stimulatory Agents:* Freund's adjuvant

- B10.BR (H-2A^k, E^k), B10.D2 (H-2A^d, E^d) and B10.S(9R) (H-2A^s, E^s) mice immunized with rec gp160 showed a proliferative response to this peptide
- KQIINMWQEVGKAMYAPPISGQIR encompasses several murine Th epitopes including KQIINMWQEVGKAMYA and is referred to as a "multideterminant region" or cluster peptide

gp160(421–436)	gp120(428–443 IIIB B10)	KQIINMWQEVGKAMYA	computer prediction	murine(H-2^{k,d,s})	[Cease1987a]

- Epitope name: T1. 1 of 2 functional epitopes identified using an amphipathic helix epitope prediction algorithm

gp160(421–436)	gp120(428–443 IIIB)	KQIINMWQEVGKAMYA	Vaccine	murine(H-2^{k,d,t4})	[Hale1989]

Vaccine: *Strain:* IIIB *HIV component:* gp160

- Epitope name: T1. Six multideterminant helper T-cell regions are recognized by mice of three or four MHC types

gp160(421–436)	gp120(428–443 IIIB)	KQIINMWQEVGKAMYA	Vaccine	murine(H-2^k)	[Ahlers1997b]

Vaccine: *Vector/type:* peptide *Strain:* IIIB *HIV component:* polyepitope

- Epitope name: T1. First identified Th epitope in HIV

- Alanine at position 436 (instead of E in wild-type) enhances MHC binding and antigenicity of peptide by several orders of magnitude
- Vaccines with a CTL epitope linked to a more potent helper epitope yielded greatly enhanced CTL response relative to the wildtype helper epitope
- T1 peptide linked to CTL epitopes in four vaccine constructs used to immunize mice: KQIINMWQEVGKAMYAPPIS-GQIRRIQRGPGRAFVTIGK, KQIINMWQEVGKAMYAPPISGQIRRIQRGPGRAFVTI, KQIINMWQAVGKAMYAPPISGQIR-RIQRGPGRAFVTIGK, KQIINMWQAVGKAMYAPPISGQIRRIQRGPGRAFVTI

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gp160(421–444) | gp160(428–451 IIIB) | KQIINMWQEVGKAMYAP-PISGQIR | HIV-1 infection, Vaccine | human, murine(H-2^k, H-2^b, H-2^s, H-2^d) | [Berzofsky1991, Berzofsky1991a]

Vaccine: *Vector/type:* recombinant protein *Strain:* IIIB *HIV component:* gp160 *Stimulatory Agents:* Freund's adjuvant

- KQIINMWQEVGKAMYAPPISGQIR encompasses several murine Th epitopes and is referred to as a "multideterminant region" or cluster peptide
- Six multideterminant region cluster peptides were evaluated Th responses in different MHC/HLA backgrounds after vaccination of mice with gp160, or in infected people
- This cluster peptide elicited proliferative responses in cells from all H-2 haplotypes tested: B10.BR mice (H-2A^k, E^k), B10.D2 mice (H-2A^d, E^d), B10.A(5R) mice (H-2A^b, E^b), and B10.S(9R) mice (H-2A^s, E^s)
- IL-2 production in response to this peptide was observed in 73% (8/11) of asymptomatic HIV-infected individuals

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gp160(421–444) | gp120(428–451 IIIB) | KQIIMNWQEVGKAMYAP-PISGQIR | Vaccine | murine(H2^d) | [Shirai1996a]

Vaccine: *Vector/type:* peptide *Strain:* IIIB

- Epitope name: T1. Linked to a CTL epitope from hepatitis C virus, induced CD4+ helper cells producing IL-2

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gp160(423–440) | gp120(428–445) | FINMWQEVGKAMYAPPIS | HIV-1 infection | human( ) | [Caruso1997]

- As HIV-1-infected individuals progress to disease, T-cells show reduced ability to proliferate in response to HIV antigen, but retain the ability to express the activation antigens CD25 and CD71
- The ability to express activation markers in response to HIV is retained, but the response to tetanus toxoid recall antigen is lost
- This study investigated CD25 and CD71 expression in PBMC from patients at various stages of progression, measuring the response to *in vitro* stimulation by peptide cocktail containing four antigenic Env peptides, or p17 and p24

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gp160(424–438) | gp120(424–438 IIIB B10) | INMWQEVGKAMYAPP | HIV-1 infection | human( ) | [Wahren1989, Wahren1989a]

- 12 gag and 18 env T-cell sites were identified that could commonly evoke T-cell responses

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gp160(425–439) | gp120(432–446 IIIB) | NMWQEVGKAMYAPPI | Vaccine | murine(H-2^{t4}) | [Hale1989]

Vaccine: *Strain:* IIIB *HIV component:* gp160

- Six multideterminant helper T-cell regions are recognized by mice of three or four MHC types

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gp160(426–440)	gp160(432–446 IIIB)	NMWQEVGKAMYAPPI	Vaccine	murine(H-2^s)	[Berzofsky1991, Berzofsky1991a]

Vaccine: *Vector/type:* recombinant protein *Strain:* IIIB *HIV component:* gp160 *Stimulatory Agents:* Freund's adjuvant

- B10.S(9R) (H-$2A^s$, E^s) mice immunized with rec gp160 showed a proliferative response to this peptide
- KQIINMWQEVGKAMYAPPISGQIR encompasses several murine Th epitopes including NMWQEVGKAMYAPPI and is referred to as a "multideterminant region" or cluster peptide

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gp160(426–441)	gp120( )	MWQEVGKAMYAPPIG-C	*in vitro* stimulation	human( )	[Manca1995b]

- Peptide stimulation of PBMC from non-infected individuals *in vitro*
- Peptide priming does not always induce T-cells that recognize whole protein

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gp160(430–444)	gp160(437–451 IIIB)	VGKAMYAPPISGQIR	Vaccine	murine(H-2^k, H-2^b, H-2^s, H-2^d)	[Berzofsky1991, Berzofsky1991a]

Vaccine: *Vector/type:* recombinant protein *Strain:* IIIB *HIV component:* gp160 *Stimulatory Agents:* Freund's adjuvant

- This peptide elicited proliferative responses in cells from all H-2 haplotypes tested: B10.BR mice (H-$2A^k$, E^k), B10.D2 mice (H-$2A^d$, E^d), B10.A(5R) mice (H-$2A^b$, E^b), and B10.S(9R) mice (H-$2A^s$, E^s)
- KQIINMWQEVGKAMYAPPISGQIR encompasses several murine Th epitopes including VGKAMYAPPISGQIR and is referred to as a "multideterminant region" or cluster peptide

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gp160(430–444)	gp120(437–451 IIIB)	VGKAMYAPPISGQIR	Vaccine	murine(H-$2^{k,d,i5,t4}$)	[Hale1989]

Vaccine: *Strain:* IIIB *HIV component:* gp160

- Six multideterminant helper T-cell regions are recognized by mice of three or four MHC types

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gp160(430–453)	gp120(430–453)	VGKAMYAPPISGQIRC-SSNITGLL	Vaccine	murine(H-2^b)	[Sjolander1996]

Vaccine: *Vector/type:* recombinant protein *HIV component:* gp160

- Study demonstrates that T-cell determinants from glycoproteins can depend on the glycosylation of the protein
- Peptide stimulation of an *in vitro* proliferative response required *in vivo* priming with glycosylated protein
- Local glycosylation sites thought not to be part of the epitope, but may be important for epitope processing

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gp160(433–447)	Env( )	AMYAPPIAGLIQCSS	Vaccine	murine(H-2 IA^b)	[Surman2001]

Vaccine: *Vector/type:* DNA, vaccinia, recombinant protein *Strain:* 1007 (clade B), UG92005 (clade D) *HIV component:* gp140 *Stimulatory Agents:* Freund's adjuvant

- This epitope is located in the C4 region of UG92005 (UG, clade D) and was recognized by ten hybridomas with Vβ usage Vβ 6, 8.1, 8.2, 13, 14 and not determined – among the ND Vβ set, three Vαs were identified, Vα 2, 8, and 11
- C57BL/6 mice were immunized with a prime-boost strategy involving three HIV-1 Env antigens: Mice were primed with DNA given i.m., 3-4 weeks later boosted with VV, and 3-4 weeks later boosted again with purified protein in Freund's adjuvant

- The vaccinia construct is a pSC11-based VV vector with the first 38 amino acids contributed by BH10 and the rest of gp120 and gp41 by the vaccine strain, the DNA construct is in the pJW4303 vector with a CMV promotor, and the purified protein is expressed from the pJW4303 vector transfected into CHO-K1 cells
- Ten days after the final boost, hybridomas were made and tested for IL-2 production using either B6 spleen cells or H-2 IA^b transfected L cells as targets and Vβ usage was determined
- Mice were immunized with an Env from either one of two clades: HIV-1 1007, a clade B strain isolated from an individual from Memphis Tennesee, and HIV-1 92UG005, a clade D strain isolated from Uganda in 1992 through the WHO
- 80 unique clonotypes were characterized from six mice
- H-2 IA^b restricted T-helper epitopes were concentrated in 5 distinct regions within the Env sequence (2 clonotype responses in V2, 26 in C2, 22 in V3, 23 in V4C4, and 7 in gp41
- Epitopes hotspots tended to be proximal to heavily glycosylated regions of the Env sequence, in exposed, non-helical strands of the protein – the non-uniform localization may be influenced by differential antigen processing and the glycosylation site proximity may allow binding to lectins and promote trafficking through processing pathways

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gp160(433–447) Env( ) SNNTVGNPIILPCRI Vaccine murine(H-2 IA^b) [Surman2001]

Vaccine: *Vector/type:* DNA, vaccinia, recombinant protein *Strain:* 1007 (clade B), UG92005 (clade D) *HIV component:* gp140 *Stimulatory Agents:* Freund's adjuvant

- This epitope is located in the V4C4 region of 1007 (US, clade B) and was recognized by 13 hybridomas with Vβ usage Vβ 4, 7, 8.1, 8.2, 10, 12 and not determined – one of the Vβ 8.2 was shown to utilize Vα 2
- C57BL/6 mice were immunized with a prime-boost strategy involving three HIV-1 Env antigens: Mice were primed with DNA given i.m., 3-4 weeks later boosted with VV, and 3-4 weeks later boosted again with purified protein in Freund's adjuvant
- The vaccinia construct is a pSC11-based VV vector with the first 38 amino acids contributed by BH10 and the rest of gp120 and gp41 by the vaccine strain, the DNA construct is in the pJW4303 vector with a CMV promotor, and the purified protein is expressed from the pJW4303 vector transfected into CHO-K1 cells
- Ten days after the final boost, hybridomas were made and tested for IL-2 production using either B6 spleen cells or H-2 IA^b transfected L cells as targets and Vβ usage was determined
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- 80 unique clonotypes were characterized from six mice
- H-2 IA^b restricted T-helper epitopes were concentrated in 5 distinct regions within the Env sequence (2 clonotype responses in V2, 26 in C2, 22 in V3, 23 in V4C4, and 7 in gp41
- Epitopes hotspots tended to be proximal to heavily glycosylated regions of the Env sequence, in exposed, non-helical strands of the protein – the non-uniform localization may be influenced by differential antigen processing and the glycosylation site proximity may allow binding to lectins and promote trafficking through processing pathways

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gp160(436–451) gp120( ) APPIGGQISCSSNITY *in vitro* stimulation human( ) [Manca1995b]

- Peptide stimulation of PBMC from non-infected individuals *in vitro*
- Peptide priming does not always induce T-cells that recognize whole protein

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gp160(438–460)	gp120(443–465 NL43)	PISGQIRCSSNITGLLL-TRDGGN	Vaccine	human( )	[Sitz1999]

Vaccine: *Vector/type:* recombinant protein *Strain:* NL43 *HIV component:* gp120, gp160

- There was a great breadth of proliferative response to Env peptides in 19 HIV-1 infected rgp160 and 17 HIV-1 infected rgp120 vaccine recipients
- Close to 40% of vaccinees had a stimulation index of greater than 5 to this peptide

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gp160(439–448)	gp120(151–160 W6.ID)	IGGQIRCSSN	Vaccine	human( )	[Jones1999]

Vaccine: *Vector/type:* recombinant protein *Strain:* W61D *HIV component:* gp120 *Stimulatory Agents:* QS21/MPL adjuvant

- HIV-1 specific T-cell lines isolated from an HIV seronegative volunteer vaccinated with rgp120 and a QS21/MPL adjuvant
- One T-cell line responds to two overlapping peptides, and the region of overlap is IGGQIRCSSN
- The IIIB version of the first reactive peptide, EVGKAMYAPPIGGQIRCSSN, has a single substitution and induces proliferation as well as the original W61D peptide : `----------S--------`

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gp160(446–461)	gp120( )	SSNITGLLLTRDGGTC	*in vitro* stimulation	human( )	[Manca1995b]

- Peptide stimulation of PBMC from non-infected individuals *in vitro*
- Peptide priming does not always induce T-cells that recognize whole protein

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gp160(456–470)	gp120( )	RDGGTNVTNDTEVFRC	*in vitro* stimulation	human( )	[Manca1995b]

- Peptide stimulation of PBMC from non-infected individuals *in vitro*
- Peptide priming does not always induce T-cells that recognize whole protein

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gp160(459–473)	gp120(459–473 IIIB B10)	GNSNNESEIFRPGGG	HIV-1 infection	human( )	[Wahren1989, Wahren1989a]

- 12 gag and 18 env T-cell sites were identified that could commonly evoke T-cell responses

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gp160(468–483)	gp120(466–481)	FRPGGGDMRDNWRSE-L	HIV-1 infection	human( )	[Krowka1990]

- Conjugation of HIV peptides to liposomes and rIL-2 stimulation may enhance cell-mediated responses

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gp160(474–488)	gp120(474–488 IIIB B10)	DMRDNWRSELYKYKV	HIV-1 infection	human( )	[Wahren1989, Wahren1989a]

- 12 gag and 18 env T-cell sites were identified that could commonly evoke T-cell responses

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gp160(476–490)	gp160(483–497 IIIB)	RDNWRSELYKYKVVK	Vaccine	murine(H-2^k, H-2^s)	[Berzofsky1991, Berzofsky1991a]

Vaccine: *Vector/type:* recombinant protein *Strain:* IIIB *HIV component:* gp160 *Stimulatory Agents:* Freund's adjuvant

- This peptide elicited proliferative responses in B10.BR mice (H-2A^k and B10.S(9R) mice (H-2A^s, E^s)
- RDNWRSELYKYKVVKIEPLGVAPT encompasses several murine Th epitopes including RDNWRSELYKYKVVK and is referred to as a "multideterminant region" or cluster peptide

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gp160(476–490) | gp120(483–497 IIIB) | RDNWRSELYKYKVVK | Vaccine | murine(H-2^{d,t4}) | [Hale1989]

Vaccine: *Strain:* IIIB *HIV component:* gp160

- Six multideterminant helper T-cell regions are recognized by mice of three or four MHC types

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gp160(476–498) | gp160(483–506 IIIB) | RDNWRSELYKYKVVK-IEPLGVAPT | HIV-1 infection, Vaccine | human, murine(H-2^k, H-2^b, H-2^s, H-2^d) | [Berzofsky1991, Berzofsky1991a]

Vaccine: *Vector/type:* recombinant protein *Strain:* IIIB *HIV component:* gp160 *Stimulatory Agents:* Freund's adjuvant

- RDNWRSELYKYKVVKIEPLGVAPT encompasses several murine Th epitopes and is referred to as a "multideterminant region" or cluster peptide
- Six multideterminant region cluster peptides were evaluated Th responses in different MHC/HLA backgrounds after vaccination of mice with gp160, or in infected people
- This cluster peptide elicited proliferative responses in cells from all H-2 haplotypes tested: B10.BR mice (H-2A^k, E^k), B10.D2 mice (H-2A^d, E^d), B10.A(5R) mice (H-2A^b, E^b), and B10.S(9R) mice (H-2A^s, E^s)
- IL-2 production in response to this peptide was observed in 52% (14/27) of asymptomatic HIV-infected individuals

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gp160(482–501) | gp120(482–501 IIIB) | ELYKYKVVKIEPLGVA-PTKA | Vaccine | Rhesus macaque( ) | [Lekutis1997a]

Vaccine: *Vector/type:* DNA *Strain:* IIIB *HIV component:* Env

- HIV-1 env DNA vaccine induced Th cell response to this epitope in a rhesus monkey
- Epitope was recognized by both monkeys used in this study

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gp160(484–496) | gp120(484–496 HXB2) | YKYKVVKIEPLGV | Vaccine | Rhesus macaque(DR*W201) | [Lekutis1998]

Vaccine: *Vector/type:* DNA *Strain:* HXB2 *HIV component:* Env

- Variants of this epitope with substitutions at position 490(K) retained ability to bind to MHC class II, but failed to induce proliferation/cytokine secretion in HIV-1 env-specific CD4+ Th cells
- The modified peptide antagonized the wildtype peptide-induced proliferative response

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gp160(484–498) | gp120(484–498 IIIB B10) | YKYKVVKIEPLGVAP | HIV-1 infection | human( ) | [Wahren1989, Wahren1989a]

- 12 gag and 18 env T-cell sites were identified that could commonly evoke T-cell responses

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gp160(484–499) | gp120(492–506 IIIB) | CKYKVVKIEPLGVAPT | Vaccine | murine(H-2^{d,k,t4,i5}) | [Hale1989]

Vaccine: *Strain:* IIIB *HIV component:* gp160

- Six multideterminant helper T-cell regions are recognized by mice of three or four MHC types

gp160(485–498)	gp160(492–506 IIIB)	KYKVVKIEPLGVAPT	Vaccine	murine(H-2^k, H-2^b, H-2^s, H-2^d)	[Berzofsky1991, Berzofsky1991a]

Vaccine: *Vector/type:* recombinant protein *Strain:* IIIB *HIV component:* gp160 *Stimulatory Agents:* Freund's adjuvant

- This peptide elicited proliferative responses in cells from all H-2 haplotypes tested: B10.BR mice (H-2A^k, E^k), B10.D2 mice (H-2A^d, E^d), B10.A(5R) mice (H-2A^b, E^b), and B10.S(9R) mice (H-2A^s, E^s)
- RDNWRSELYKYKVVKIEPLGVAPT encompasses several murine Th epitopes including KYKVVKIEPLGVAPT and is referred to as a "multideterminant region" or cluster peptide

gp160(485–500)	gp120( )	KYKVIKIEPLGIAPTC	*in vitro* stimulation	human( )	[Manca1995b]

- Peptide stimulation of PBMC from non-infected individuals *in vitro*
- Peptide priming does not always induce T-cells that recognize whole protein

gp160(486–494)	gp120(486–494 IIIB)	YKVVKIEPL	SHIV infection	Rhesus macaque(DRB*W201)	[Lekutis1997b]

- C5 region minimal epitope determined through fine epitope mapping

gp160(487–512)	gp120(494–518 IIIB)	KVVKIEPLGVAPTKAK-RRVVQREKRC	Vaccine	murine( )	[Goodman-Snitkoff1990]

Vaccine: *Vector/type:* peptide *Strain:* IIIB

- Identification of putative Th epitopes that stimulate an antibody response in peptide immunized mice

gp160(499–511)	gp120( )	TKAKRRVVEREKR	*in vitro* stimulation	human(DR)	[Wilson1997a]

- Thought to be a mimic of a HLA class II DR β chain variable region
- Response to this epitope may cause a breakdown of self-tolerance
- Presentation of epitope induced autoreactive T-cell lines in PBMC from uninfected donors
- Suppression of proliferation to soluble antigens by the CD8+ fraction of TKAKRRVVEREKR stimulated T-cells was observed

gp160(519–543)	Env(519–543)	FLGFLGAAGSTMGAA-SLTLTVQARC	Vaccine	Rhesus macaque( )	[Nehete1993]

Vaccine: *Vector/type:* peptide

- Synthetic peptide derived from conserved region of the HIV-1 envelope that stimulates a proliferative response in mice, and in rhesus monkeys
- Proliferative response to this peptide was observed in 3/3 immunized rhesus monkeys

gp160(519–543)	Env(519–543)	FLGFLGAAGSTMGAA-SLTLTVQARQ	HIV-1 infection	human, chimpanzee( )	[Nehete1998a]

- HIV-infected chimpanzees and HIV-positive patients show positive proliferative responses to multiple peptides from five conserved regions of the HIV-1 Env

gp160(519–543)	gp41(519–543)	FLGFLGAAGSTMGAA-SLTLTVQARC	Vaccine	murine(H-$2^{bxk,sxd}$)	[Sastry1991]

Vaccine: *Vector/type:* peptide

- Peptides induced T-cell proliferative response to immunizing peptide and to gp160

gp160(547–561)	gp41(547–561 IIIB B10)	GIVQQQNNLLRAIEA	HIV-1 infection	human( )	[Wahren1989, Wahren1989a]

- 12 gag and 18 env T-cell sites were identified that could commonly evoke T-cell responses

gp160(562–576)	gp41(562–576 IIIB B10)	QQHLLQLTVWGIKQL	HIV-1 infection	human( )	[Wahren1989, Wahren1989a]

- 12 gag and 18 env T-cell sites were identified that could commonly evoke T-cell responses

gp160(572–591)	gp41(572–591)	GIKQLQARILAVERYL-KDQQ	Vaccine	murine(H-$2^{d,b}$)	[Brown1995]

Vaccine: *Vector/type:* peptide

- This peptide was a good immunogen in BALB/c and CBA mice, producing a strong proliferative response
- At least one of the four residues GIKQ enhances stimulation, and in CBA mice these residues influence the ability to prime T-cells *in vivo*
- QLQARILAVERY stimulated the greatest *in vitro* T-cell response
- VERYLKDQQ was the minimal reactive sequence recognized by a T-cell line

gp160(576–591)	gp41(576–591)	LQARILAVERYLKDQQ	Vaccine	murine(H-$2^{d,b}$)	[Brown1995]

Vaccine: *Vector/type:* peptide

- This peptide was a poor immunogen in BALB/c and CBA mice used in this experiment, producing a weak proliferative response

gp160(578–608)	gp41(585–615 IIIB)	ARILAVERYLKDQQLL-GIWGCSGKLICTTAV	Vaccine	murine( )	[Goodman-Snitkoff1990]

Vaccine: *Vector/type:* peptide

- Identification of putative Th epitopes that can stimulate an antibody response in peptide immunized mice

gp160(579–601)	gp41(579–601)	RILAVERYLKDQQLLG-GIWGCSGK	Vaccine	murine(H-$2^{d,b}$)	[Brown1995]

Vaccine: *Vector/type:* peptide

- This peptide was a good immunogen in BALB/c and CBA
- This peptide produced a strong Th response in both mice strains which was more responsive towards GIKQLQARILAVERYLKDQQ and LQARILAVERYLKDQQ than to immunizing peptide

gp160(579–604)	gp41(584–609 LAI)	RILAVERYLKDQQLLG-IWGCSGKLIC	HIV-1 infection	human( )	[Schrier1989]
• Stimulates T-cell proliferation in HIV-infected donors					
gp160(586–597)	Env(586–598)	YLRDQQLLGIWG	HIV-1 infection	human, chimpanzee( )	[Nehete1998a]
• HIV-infected chimpanzees and HIV-positive patients show positive proliferative responses to multiple peptides from five conserved regions of the HIV-1 Env					
gp160(586–598)	Env(586–598)	YLRDQQLLGIWGC	Vaccine	murine, Rhesus macaque( )	[Nehete1993]
Vaccine: *Vector/type:* peptide					
• Synthetic peptide derived from conserved region of the HIV-1 envelope that stimulates a proliferative response in mice					
• Proliferative response to this peptide was observed in 1/3 immunized rhesus monkeys, with a weak transient response in the other two					
gp160(593–604)	gp41(593–604 IIIB)	LGIWGCSGKLIC	HIV-1 infection	human( )	[Bell1992]
• Elicits T-cell proliferation and B cell responses, but only during the asymptomatic phase of HIV infection					
gp160(593–604)	gp41(598–609 LAV-1)	LGLWGCSGKLIC	Vaccine	murine($H2^d$)	[Schrier1988]
• Murine T-dependent B-cell response – 7/29 had a proliferative response to this peptide					
gp160(594–603)	gp41(594–603 IIIB)	GIWGCSGKLI	HIV-1 infection	human( )	[Kelleher1998]
• Epitope documented as a "previously described" epitope [Bell1992], but in Bell *et al.* it was described as gp41(594-603 IIIB), LGIWGCSGKLIC					
• Immunization with a p24-VLP virus-like particle did not significantly impact CD4+ lymphocyte count, viral load, or p24 antibody titre					
• Immunization with p24-VLP did not increase the proliferative response to this gp41 epitope, however, there was a modest, short-lived increased proliferative response to p24					
gp160(594–604)	gp41( )	GIWGCSGKLIC	HIV-1 infection	human( )	[Mutch1994]
• Core region of peptides that can stimulate proliferative responses from seronegative and seropositive people					
gp160(598–609)	gp41(603–614 LAI)	CSGKLICTTAVP	HIV-1 infection	human( )	[Schrier1989]
• Stimulates T-cell proliferation in HIV-infected donors					
gp160(604–615)	gp41(609–620 LAI)	CTTAVPWNASWS	HIV-1 infection	human( )	[Schrier1989]
• Stimulates T-cell proliferation in HIV-infected donors					

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
gp160(606–620)	gp41( )	TNVPWNASWSNKSLE	Vaccine	murine(H-2 IA^b)	[Surman2001]

Vaccine: *Vector/type:* DNA, vaccinia, recombinant protein *Strain:* 1007 (clade B), UG92005 (clade D) *HIV component:* gp140 *Stimulatory Agents:* Freund's adjuvant

- This gp140 epitope of UG92005 (UG, clade D) was recognized by five hybridomas with Vβ usage Vβ 8.1, 14 and not determined – one of the Vβ 8.1 was shown to utilize Vα 8
- C57BL/6 mice were immunized with a prime-boost strategy involving three HIV-1 Env antigens: Mice were primed with DNA given i.m., 3-4 weeks later boosted with VV, and 3-4 weeks later boosted again with purified protein in Freund's adjuvant
- The vaccinia construct is a pSC11-based VV vector with the first 38 amino acids contributed by BH10 and the rest of gp120 and gp41 by the vaccine strain, the DNA construct is in the pJW4303 vector with a CMV promotor, and the purified protein is expressed from the pJW4303 vector transfected into CHO-K1 cells
- Ten days after the final boost, hybridomas were made and tested for IL-2 production using either B6 spleen cells or H-2 IA^b transfected L cells as targets and Vβ usage was determined
- Mice were immunized with an Env from either one of two clades: HIV-1 1007, a clade B strain isolated from an individual from Memphis Tennesee, and HIV-1 92UG005, a clade D strain isolated from Uganda in 1992 through the WHO
- 80 unique clonotypes were characterized from six mice
- H-2 IA^b restricted T-helper epitopes were concentrated in 5 distinct regions within the Env sequence (2 clonotype responses in V2, 26 in C2, 22 in V3, 23 in V4C4, and 7 in gp41
- Epitopes hotspots tended to be proximal to heavily glycosylated regions of the Env sequence, in exposed, non-helical strands of the protein – the non-uniform localization may be influenced by differential antigen processing and the glycosylation site proximity may allow binding to lectins and promote trafficking through processing pathways

gp160(609–616)	gp41( )	PWNASWSN	HIV-1 infection	human( )	[Mutch1994]

- Core region of peptides that can stimulate proliferative responses from seronegative and seropositive people

gp160(611–620)	gp41( )	NASWSNKSLE	Vaccine	murine(H-2 IA^b)	[Surman2001]

Vaccine: *Vector/type:* DNA, vaccinia, recombinant protein *Strain:* 1007 (clade B), UG92005 (clade D) *HIV component:* gp140 *Stimulatory Agents:* Freund's adjuvant

- This gp41 epitope is conserved in 1007 (US, clade B) and UG92005 (UG, clade D) and was recognized by two hybridomas from two different mice that were vaccinated with different clades – the Vβ usage was Vβ 4 and 14
- The epitope described here is the region of overlap of two 15 mers that were both able to stimulate IL-2 production from the hybridoma (T[TN]VPWNASWSNKSLE and NASWSNKSLEQIWNN) – the only difference between 1007 and UG92005 for these two proteins is that 1007 has a T and UG92005 has an N in the second position of the first peptide
- C57BL/6 mice were immunized with a prime-boost strategy involving three HIV-1 Env antigens: Mice were primed with DNA given i.m., 3-4 weeks later boosted with VV, and 3-4 weeks later boosted again with purified protein in Freund's adjuvant
- The vaccinia construct is a pSC11-based VV vector with the first 38 amino acids contributed by BH10 and the rest of gp120 and gp41 by the vaccine strain, the DNA construct is in the pJW4303 vector with a CMV promotor, and the purified protein is expressed from the pJW4303 vector transfected into CHO-K1 cells

- Ten days after the final boost, hybridomas were made and tested for IL-2 production using either B6 spleen cells or H-2 IA^b transfected L cells as targets and Vβ usage was determined
- Mice were immunized with an Env from either one of two clades: HIV-1 1007, a clade B strain isolated from an individual from Memphis Tennesee, and HIV-1 92UG005, a clade D strain isolated from Uganda in 1992 through the WHO
- 80 unique clonotypes were characterized from six mice
- H-2 IA^b restricted T-helper epitopes were concentrated in 5 distinct regions within the Env sequence (2 clonotype responses in V2, 26 in C2, 22 in V3, 23in V4C4, and 7 in gp41
- Epitopes hotspots tended to be proximal to heavily glycosylated regions of the Env sequence, in exposed, non-helical strands of the protein – the non-uniform localization may be influenced by differential antigen processing and the glycosylation site proximity may allow binding to lectins and promote trafficking through processing pathways

gp160(614–629)	gp41( )	WSNKSLEDIWDNMTW-C	*in vitro* stimulation	human( )	[Manca1995b]

- Peptide stimulation of PBMC from non-infected individuals *in vitro*
- Peptide priming does not always induce T-cells that recognize whole protein

gp160(634–649)	gp41( )	EIDNYTNTIYTLLEEC	*in vitro* stimulation	human( )	[Manca1995b]

- Peptide stimulation of PBMC from non-infected individuals *in vitro*
- Peptide priming does not always induce T-cells that recognize whole protein

gp160(647–661)	gp41(647–661 IIIB B10)	EESQNQQEKNEQELL	HIV-1 infection	human( )	[Wahren1989, Wahren1989a]

- 12 gag and 18 env T-cell sites were identified that could commonly evoke T-cell responses

gp160(650–662)	gp41(655–667 LAI)	QNQQEKNEQELLE	HIV-1 infection	human( )	[Schrier1989]

- Stimulates T-cell proliferation in HIV-infected donors

gp160(667–681)	gp41(667–681 IIIB B10)	ASLWNWFNITNWLWY	HIV-1 infection	human( )	[Wahren1989, Wahren1989a]

- 12 gag and 18 env T-cell sites were identified that could commonly evoke T-cell responses

gp160(682–696)	gp41(682–696 IIIB B10)	IKLFIMIVGGLVGLR	HIV-1 infection	human( )	[Wahren1989, Wahren1989a]

- 12 gag and 18 env T-cell sites were identified that could commonly evoke T-cell responses

gp160(724–745)	gp41(731–752)	PRGPDRPEGIEEEGGE-RDRDRS	Vaccine	murine(H-2k)	[McInerney1999]

Vaccine: *Vector/type:* peptide in cowpea mosaic virus (CPMV) *HIV component:* gp41 *Stimulatory Agents:* adjuvant Quil A

- A gp41 peptide was expressed in a cowpea mosaic virus (CPMV) and mice were vaccinated with a purified chimeric particle – out of five adjuvants tested, only Quil A could stimulate anti-gp41 antibodies and an *in vitro* proliferative response

- The antibodies were predominantly IgG2a, suggesting a Th1 response

gp160(732–744)	gp41(737–749 LAI)	GIEEEGGERDRDR	HIV-1 infection	human( )	[Schrier1989]

- Stimulates T-cell proliferation in HIV-infected donors

gp160(780–794)	gp160(787–801 IIIB)	RIVELLGRRGWEALK	Vaccine	murine(H-2^k, H-2^d, H-2^s)	[Berzofsky1991, Berzofsky1991a]

Vaccine: *Vector/type:* recombinant protein *Strain:* IIIB *HIV component:* gp160 *Stimulatory Agents:* Freund's adjuvant

- This peptide elicited proliferative responses in cells from B10.BR mice (H-2A^k, E^k), B10.D2 mice (H-2A^d, E^d), and B10.S(9R) mice (H-2A^s, E^s)
- RIVELLGRRGWEALKYWWNLLQYWSQELKNSAVS encompasses several murine Th epitopes including RIVELLGRRGWEALK and is referred to as a "multideterminant region" or cluster peptide, but the longer peptide only stimulates cells from H-2^k mice

gp160(780–794)	gp41(787–801 IIIB)	RIVELLGRRGWEALK	Vaccine	murine(H-2^{d,k,t4})	[Hale1989]

Vaccine: *Strain:* IIIB *HIV component:* gp160

- Six multideterminant helper T-cell regions are recognized by mice of three or four MHC types

gp160(780–813)	gp160(787–820 IIIB)	RIVELLGRRGWEALK-YWWNLLQYWSQELKNS-AVS	HIV-1 infection, Vaccine	murine(H-2^k)	[Berzofsky1991, Berzofsky1991a]

Vaccine: *Vector/type:* recombinant protein *Strain:* IIIB *HIV component:* gp160 *Stimulatory Agents:* Freund's adjuvant

- RIVELLGRRGWEALKYWWNLLQYWSQELKNSAVS encompasses several murine Th epitopes and is referred to as a "multideterminant region" or cluster peptide
- Six multideterminant region cluster peptides were evaluated Th responses in different MHC/HLA backgrounds after vaccination of mice with gp160, or in infected people
- This cluster peptide elicited proliferative responses in cells from only B10.BR mice (H-2A^k, E^k), and not from B10.D2 mice (H-2A^d, E^d), B10.A(5R) mice (H-2A^b, E^b), or B10.S(9R) mice (H-2A^s, E^s)
- IL-2 production in response to this peptide was observed in 59% (17/29) of asymptomatic HIV-infected individuals

gp160(794–808)	gp160(801–815 IIIB)	KYWWNLLQYWSQELK	Vaccine	murine(H-2^k, H-2^d, H-2^s)	[Berzofsky1991, Berzofsky1991a]

Vaccine: *Vector/type:* recombinant protein *Strain:* IIIB *HIV component:* gp160 *Stimulatory Agents:* Freund's adjuvant

- This peptide elicited proliferative responses in cells from B10.BR mice (H-2A^k, E^k), B10.D2 mice (H-2A^d, E^d), and B10.S(9R) mice (H-2A^s, E^s)
- RIVELLGRRGWEALKYWWNLLQYWSQELKNSAVS encompasses several murine Th epitopes including KYWWNLLQYWSQELK and is referred to as a "multideterminant region" or cluster peptide, but the longer peptide only stimulates cells from H-2^k mice

gp160(794–808)	gp41(801–815 IIIB)	KYWWNLLQYWSQELK	Vaccine	murine(H-2^k)	[Hale1989]

Vaccine: *Strain:* IIIB *HIV component:* gp160

- Six multideterminant helper T-cell regions are recognized by mice of three or four MHC types

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gp160(799–813)	gp160(806–820 IIIB)	LLQYWSQELKNSAVS	Vaccine	murine(H-2^k, H-2^d, H-2^s)	[Berzofsky1991, Berzofsky1991a]

Vaccine: *Vector/type:* recombinant protein *Strain:* IIIB *HIV component:* gp160 *Stimulatory Agents:* Freund's adjuvant

- This peptide elicited proliferative responses in cells from B10.BR mice (H-2A^k, E^k), B10.D2 mice (H-2A^d, E^d), and B10.S(9R) mice (H-2A^s, E^s)
- RIVELLGRRGWEALKYWWNLLQYWSQELKNSAVS encompasses several murine Th epitopes including LLQYWSQELKNSAVS and is referred to as a "multideterminant region" or cluster peptide, but the longer peptide only stimulates cells from H-2^k mice

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gp160(799–813)	gp41(806–820 IIIB)	LLQYWSQELKNSAVS	Vaccine	murine(H-$2^{k,d,t4}$)	[Hale1989]

Vaccine: *Strain:* IIIB *HIV component:* gp160

- Six multideterminant helper T-cell regions are recognized by mice of three or four MHC types

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gp160(799–813)	gp41(806–820 IIIB)	LLQYWSQELKNSAVS	Vaccine	murine(H-$2^{k,d,t4}$)	[Hale1989]

Vaccine: *Strain:* IIIB *HIV component:* gp160

- Six multideterminant helper T-cell regions are recognized by mice of three or four MHC types

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gp160(814–829)	gp41( )	WLNATAIAVTEGTDRC	*in vitro* stimulation	human( )	[Manca1995b]

- Peptide stimulation of PBMC from non-infected individuals *in vitro*
- Peptide priming does not always induce T-cells that recognize whole protein

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gp160(821–835)	gp160(828–842 IIIB)	AVAEGTDRVIEVVQG	Vaccine	murine(H-2^k, H-2^b, H-2^s)	[Berzofsky1991, Berzofsky1991a]

Vaccine: *Vector/type:* recombinant protein *Strain:* IIIB *HIV component:* gp160 *Stimulatory Agents:* Freund's adjuvant

- This peptide elicited proliferative responses in cells from B10.BR mice (H-2A^k, E^k), B10.A(5R) mice (H-2A^b, E^b), and B10.S(9R) mice (H-2A^s, E^s)
- AVAEGTDRVIEVVQGAYRAIRHIPRRIRQGLER encompasses several murine Th epitopes including AVAEGTDRVIEVVQG and is referred to as a "multideterminant region" or cluster peptide

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gp160(821–835)	gp41(828–842 IIIB)	AVAEGTDRVIEVVQG	Vaccine	murine(H-2^k)	[Hale1989]

Vaccine: *Strain:* IIIB *HIV component:* gp160

- Six multideterminant helper T-cell regions are recognized by mice of three or four MHC types

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gp160(821–838)	gp41(827–843)	YVAEGTDRVIEVVQG-ACR	HIV-1 infection	human( )	[Caruso1997]

- As HIV-1-infected individuals progress to disease, T-cells show reduced ability to proliferate in response to HIV antigen, but retain the ability to express the activation antigens CD25 and CD71
- The ability to express activation markers in response to HIV is retained, but the response to tetanus toxoid recall antigen is lost
- This study investigated CD25 and CD71 expression in PBMC from patients at various stages of progression, measuring the response to *in vitro* stimulation by peptide cocktail containing four antigenic Env peptides, or p17 and p24

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gp160(821–853) gp160(828–860 IIIB) AVAEGTDRVIEVVQGAYRAIRHIPRRIRQGLER HIV-1 infection, Vaccine human, murine(H-2^k, H-2^b, H-2^s, H-2^d) [Berzofsky1991, Berzofsky1991a]

Vaccine: *Vector/type:* recombinant protein *Strain:* IIIB *HIV component:* gp160 *Stimulatory Agents:* Freund's adjuvant

- AVAEGTDRVIEVVQGAYRAIRHIPRRIRQGLER encompasses several murine Th epitopes and is referred to as a "multideterminant region" or cluster peptide
- Six multideterminant region cluster peptides were evaluated for Th responses in different MHC/HLA backgrounds after vaccination of mice with gp160, or in infected people
- This cluster peptide elicited proliferative responses in cells from all four MHC types tested: B10.BR mice (H-$2A^k$, E^k), B10.D2 mice (H-$2A^d$, E^d), B10.A(5R) mice (H-$2A^b$, E^b), and B10.S(9R) mice (H-$2A^s$, E^s)
- IL-2 production in response to this peptide was observed in only 8% (1/12) of asymptomatic HIV-infected individuals

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gp160(827–835) gp41(834–842 IIIB) DRVIEVVQG Vaccine murine(H-2^k) [Hale1989]

Vaccine: *Strain:* IIIB *HIV component:* gp160

- Suggested epitope based on region of overlap

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gp160(827–841) gp41(834–848 IIIB) DRVIEVVQGAYRAIR Vaccine Rhesus macaque( ) [Hosmalin1991]

Vaccine: *Vector/type:* peptide prime with protein boost *Strain:* IIIB *HIV component:* gp160

- Epitope name: TH4. Peptide priming to induce T-cell help enhances antibody response to gp160 immunization
- Called Th4.1 and TH4

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gp160(827–841) gp41(834–848 IIIB) DRVIEVVQGAYRAIR HIV-1 infection human( ) [Clerici1997]

- Epitope name: TH4. Used in a study of the influence of pentoxifylline on HIV specific T-cells

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gp160(827–841) gp41(834–848 IIIB) DRVIEVVQGAYRAIR HIV-1 exposed seronegative human( ) [Pinto1995a]

- Epitope name: TH4. CTL activity analyzed in parallel with Th reactivity in exposed but uninfected health care workers
- Called Th4.1 and TH4

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gp160(827–841) gp41(834–848 IIIB) DRVIEVVQGAYRAIR HIV-1 infection human( ) [Clerici1991a]

- Epitope name: TH4. Peptides stimulate Th cell function and CTL activity in similar patient populations
- Called Th4.1 and TH4

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gp160(827–841) gp41(834–848 IIIB) DRVIEVVQGAYRAIR Vaccine human( ) [Clerici1991b]

Vaccine: *Vector/type:* recombinant protein *Strain:* IIIB *HIV component:* gp160

- Epitope name: TH4. Immunizing uninfected individuals with rgp160 results in stronger Th response than does natural infection
- Called Th4.1 and TH4

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gp160(827–841) gp41(834–848 IIIB) DRVIEVVQGAYRAIR HIV-1 exposed seronegative human( ) [Clerici1992]

- Epitope name: TH4. Cell-mediated immune response to HIV-1 peptides in HIV-1 exposed seronegative men
- Called Th4.1 and TH4

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gp160(827–841) gp41(834–848 IIIB) DRVIEVVQGAYRAIR HIV-1 infection human( ) [Clerici1989]

- Epitope name: TH4. IL-2 production detection of Th lymphocytes from asymptomatic HIV-positive individuals
- Called Th4.1 and TH4

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gp160(827–841) gp41(834–848 IIIB) DRVIEVVQGAYRAIR HIV-1 infection human( ) [Kaul1999a]

- Epitope name: TH4. Kenyan sex workers that remained seronegative were found to frequently have HIV-env peptide specific Th responses detected by an IL-2 assay (11/20 cases) and mucosal genital tract anti-HIV IgA (16/21 cases)
- The helper epitopes used in this study were noted to be previously described [Clerici1989], and were not explicitly described in [Kaul1999a]

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gp160(827–841) gp41( ) DRVIEVVQGAYRAIR HIV-1 exposed seronegative, HIV-1 infection human( ) [Kuhn2001]

- Epitope name: TH4, Th4.1. In a S. African perinatal transmission study, 33% (33/86) of cord blood samples from infants with seropositive mothers produced T-helper responses (measured by a bioassay measuring IL-2 production in a murine cell line and confirmed with a proliferation assay) against a peptide cocktail containing Th epitopes P18 MN, P18 IIIB, T1, T2, and TH4
- The mothers were predominantly infected subtype C but the T-helper response was detectable in a number of cord blood samples despite using peptides based on B subtype reagents
- 3/33 infants with cord blood T-helper responses to Env were infected *in utero*, 2/33 were lost to follow up, and 28/33 were not infected – 6/53 of the infants with cord blood that was unresponsive to Env peptide stimulation were infected before delivery, and 8/47 contracted HIV intrapartum or via breast-feeding
- Measurable HIV specific T-helper responses elicited in the immunologically immature newborn, possibly in response to *in utero* exposure, are associated with a protective natural immunity that helps block mother-infant transmission of HIV-1

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gp160(827–841) gp160(834–848 IIIB) DRVIEVVQGAYRAIR Vaccine murine(H-2^{k}, H-2^{b}) [Berzofsky1991, Berzofsky1991a]

Vaccine: *Vector/type:* recombinant protein *Strain:* IIIB *HIV component:* gp160 *Stimulatory Agents:* Freund's adjuvant

- This peptide elicited proliferative responses in cells from B10.BR mice (H-2A^{k}, E^{k}) and B10.A(5R) mice (H-2A^{b}, E^{b})

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gp160(827–841) gp41(834–848 IIIB) DRVIEVVQGAYRAIR Vaccine murine(H-2^{k,i5}) [Hale1989]

Vaccine: *Strain:* IIIB *HIV component:* gp160

- Epitope name: TH4. Six multideterminant helper T-cell regions are recognized by mice of three or four MHC types
- Called Th4.1 and TH4

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gp160(829–837)	gp160(836–850 IIIB)	VIEVVQGAYRAIRHI	Vaccine	murine(H-2^k, H-2^b)	[Berzofsky1991, Berzofsky1991a]

Vaccine: *Vector/type:* recombinant protein *Strain:* IIIB *HIV component:* gp160 *Stimulatory Agents:* Freund's adjuvant

- This peptide elicited proliferative responses in cells from B10.BR mice (H-2A^k, E^k) and B10.A(5R) mice (H-2A^b, E^b)

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gp160(834–841)	gp41(841–848 IIIB)	QGAYRAIR	Vaccine	murine(H-2^{i5})	[Hale1989]

Vaccine: *Strain:* IIIB *HIV component:* gp160

- Suggested H-2^k epitope based on region of overlap

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gp160(834–848)	gp160(841–855 IIIB)	QGAYRAIRHIPRRIR	Vaccine	murine(H-2^k, H-2^b, H-2^d, H-2^s)	[Berzofsky1991, Berzofsky1991a]

Vaccine: *Vector/type:* recombinant protein *Strain:* IIIB *HIV component:* gp160 *Stimulatory Agents:* Freund's adjuvant

- This peptide elicited proliferative responses in cells from B10.BR mice (H-2A^k, E^k), B10.A(5R) mice (H-2A^b, E^b), B10.D2(H-2A^d, E^d), and B10.S(9R) mice (H-2A^s, E^s)

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gp160(834–848)	gp41(841–855 IIIB)	QGAYRAIRHIPRRIR	Vaccine	murine(H-2^{d,t4,i5})	[Hale1989]

Vaccine: *Strain:* IIIB *HIV component:* gp160

- Six multideterminant helper T-cell regions are recognized by mice of three or four MHC types

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gp160(839–848)	gp41(846–855 IIIB)	AIRHIPRRIR	Vaccine	murine(H-2^{d,t4})	[Hale1989]

Vaccine: *Strain:* IIIB *HIV component:* gp160

- Suggested H-2^{d,t4} epitope based on region of overlap

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gp160(839–853)	gp160(828–842 IIIB)	AIRHIPRRIRQGLER	Vaccine	human, murine(H-2^k, H-2^b, H-2^s)	[Berzofsky1991, Berzofsky1991a]

Vaccine: *Vector/type:* recombinant protein *Strain:* IIIB *HIV component:* gp160 *Stimulatory Agents:* Freund's adjuvant

- This peptide elicited proliferative responses in cells from B10.BR mice (H-2A^k, E^k), B10.A(5R) mice (H-2A^b, E^b), and B10.S(9R) mice (H-2A^s, E^s)

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gp160(839–853)	gp41(846–860 IIIB)	AIRHIPRRIRQGLER	Vaccine	murine(H-2^{d,t4})	[Hale1989]

Vaccine: *Strain:* IIIB *HIV component:* gp160

- Six multideterminant helper T-cell regions are recognized by mice of three or four MHC types

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gp160(842–856)	gp41(842–856 IIIB B10)	HIPRRIRQGLERILL	HIV-1 infection	human( )	[Wahren1989, Wahren1989a]

- 12 gag and 18 env T-cell sites were identified that could commonly evoke T-cell responses

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